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Chemical Testing Industry Profile of Toxicological Testing

Development Planning and Research
Associates, Inc., Manhattan, KS

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CHEMICAL TESTING INDUSTRY
PROFILE OF TOXICOLOGICAL TESTING

Prepared for:

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDES AND TOXIC SUBSTANCES
WASHINGTON, D.C. 20460

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The study assists the EPA in evaluating the foreseeable availability of the facilities and personnel needed to perform the toxicological testing required under the Toxic Substances Control Act. The study profiles the toxicological testing industry which is estimated to contain 285 commercial toxicology laboratories with average employment of 57 per laboratory and average laboratory space, 28,000 sq. ft. Annual revenues for the industry are estimated at $650 million or $2.3 million per laboratory and market competition is high with no individual firm or small group of firms controlling key resources. The current supply of testing resources is adequate with industry utilization at about 80 to 85 percent. Capital and professional manpower are key resources. Demand for testing and testing resources should be strong and arises from regulatory sources including TSCA, FIFRA and FFDCA and non-regulatory sources. Finally, a conceptual supply/demand model shows it is possible to simulate and assess the potential economic impacts of regulatory changes as well as changes in prices, availability of resources and industry structure, but data and resource requirements to implement such a model would be substantial.

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PREFACE

The attached document is a contractor's study done with the supervision and review of the Office of Pesticides and Toxic Substances of the U.S. Environmental Protection Agency. The purpose of the study is to establish an economic profile of the chemical testing industry, emphasizing the toxicological testing segment.

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CONTENTS

Page

PREFACE iii

EXECUTIVE SUMMARY 1

I. INTRODUCTION I-1
  A. Background I-1
  B. Scope of the Analysis I-2
  C. General Approach I-4

II. LITERATURE AND DATA REVIEW II-1
  A. Industry Structure and Organization II-1
  B. Literature/Data Review II-2
  C. Data Sources and Limitations II-4

III. THE TOXICOLOGICAL TESTING INDUSTRY AND SUPPLY OF TESTING RESOURCES III-1
  A. Profile of the Toxicological Testing Industry III-2
  B. Testing Capabilities III-12
  D. Resource Supplies and Constraints III-22

IV. DEMAND FOR TOXICOLOGICAL TESTING IV-1
  A. Methodology of Demand Assessment IV-2
  B. Demand for Pesticide Testing under FIFRA IV-3
  C. Demand for Toxicological Testing Under TSCA IV-12
  D. Demand for Toxicological Testing Under FFDCA IV-21
  E. Commercial Demand for Testing not Directly Induced by Regulation IV-43
  F. Research Demand for Toxicological Testing IV-43
  G. Summary: Demand for Resources Used in Toxicological Testing IV-44

V. CONCEPTUAL SUPPLY-DEMAND MODEL DEVELOPMENT V-1
  A. Analytical System V-2
  B. Supply Module V-6
  C. Demand Module V-7
  D. An Accounting Subsystem V-8
  E. An Economic Subsystem V-15
  F. General Implementation Requirements V-20
  G. Research Implications V-27

VI. REFERENCES VI-1

APPENDIX A - LISTING OF TOXICOLOGICAL TESTING LABORATORIES
APPENDIX B - TOXICOLOGY LABORATORY CONTACT FORM AND TELEPHONE SURVEY INSTRUMENT

CHEMICAL TESTING INDUSTRY: PROFILE OF TOXICOLOGICAL TESTING

EXECUTIVE SUMMARY

The Toxic Substances Control Act (TSCA) of 1976 requires that all chemical substances which may present unreasonable risks to either health or the environment shall be tested for their toxicological effects. Under Section 4 of TSCA, the Administrator of the Environmental Protection Agency (EPA) is to promulgate rules for the obtaining of health and environmental effects data and is to consider:

> "...the reasonably foreseeable availability of the facilities and personnel needed to perform the testing required under the rule (Subsection 4b(1))."

That latter consideration provided the impetus for this chemical testing industry study--the primary purpose of which is to assess the capacity and resources of the toxicological testing industry in relation to the demands made upon that industry with and without TSCA's additional testing requirements.

The two main objectives of this study are: (1) to develop an economic profile of the toxicological testing industry--its supply and demand attributes, and (2) to prepare a list of laboratories that supply the industry's services. Initially the study depended entirely upon secondary data; however, when such were found to be inadequate, the study team conducted a survey of the chemical testing industry's laboratories and facilities to broaden that data base. Various data limitations are still pronounced, and these are documented in industry and research literature and noted in this report.

The study's economic profile analysis includes three major parts: (1) an assessment of the toxicological testing industry and the availability of its key testing resources, (2) the identification of aggregate regulatory and nonregulatory resource demands (including non-testing resource uses), and (3) the development of a resource-based supply-demand model. A listing of confirmed toxicology laboratories was also prepared from a telephone survey of laboratories (Appendix A).

Both existing and new chemical substances may require toxicological effects testing under the provisions of TSCA. Although the precise magnitude of the overall testing that will be required is unknown, the complexity of the task is suggested by the fact that some 55,000 chemical substances are currently on TSCA's inventory of chemical substances and additional substances, many requiring testing, are regularly introduced by both private and public developers.

Although not all chemicals do or will require extensive testing, the industry's anticipation of increased testing requirements has prompted the rapid expansion of testing facilities in recent years. During this expansion period, professional and technical personnel were in relatively short supply. Current personnel numbers appear adequate relative to present testing levels, however.

The review of available literature and secondary data sources provided a basis for segmenting and characterizing, in general terms, the chemical testing industry. Based upon this review, the chemical testing industry was divided into three segments: biological, environmental, and product chemistry. Due to the nature of tests included in each category, resource competition between these segments appears minimal. Toxicological testing encompasses both environmental and biological chemistry testing; however, biological (animal) chemistry testing was the main focus of this study because of TSCA's potential demands upon this specific industry's resources and the probable constraints that will be posed.

Two previous studies (ICF, 1980; Enviro Control, 1980) of the chemical testing industry provided the following observations that were determinative within this present study:

- Professional manpower was a critical resource constraint to testing supply.
- Laboratory space, capital, and equipment were potential resource constraints.
- Testing laboratories, reporting widely varied price estimates for tests, apparently compete on factors other than price.

Review of other sources (e.g., periodicals) supported the above observations and provided additional evidence for the following:

- Testing capacity is potentially insufficient.
- Mutagenicity testing research may yield new methods for testing and screening and, consequently, may favorably alter the industry's potential to meet increased demand.
- The chemical testing industry includes four categories of laboratories: independent, in-house (company), university and government.

Data limitations were found for measuring both supply and demand. Supply sources include various incomplete laboratory lists which, additionally, do not generally provide information on facility capacity and capability. Too, these sources are outdated and unverified. A few sources on manpower were available. Some demand sources were available for characterizing regulatory demand by Agency and Act, but little data on nonregulatory (private) demand were found.

Supply of Testing Resources

This study's assessment of the toxicological testing supply includes descriptions of the industry and the major groups of its laboratories, characterizes capacity utilization in the industry, and analyzes the availability of industry resources.

The surveying of a screening list of potential toxicology laboratories provided an estimate of 280 to 290 laboratories performing commercial toxicological testing. (For the study's analytical purposes, a population estimate of 285 was used.) These primarily included independent contract laboratories and captive laboratories. Some university laboratories that indicated the ability or desire to do commercial toxicological testing were also included. (Other universities may also operate toxicology laboratories, but these, because they are primarily used for teaching or basic research, were excluded.) Other sources of testing supply--government and foreign laboratories--were considered less significant contributors to testing supply and outside the scope of this report; therefore, they received only limited examination.

The survey also provided extensive and, heretofore, unavailable information on toxicology laboratories. Some of the more general findings were that

- 34 percent of the laboratories were independents and 66 percent were captives (including universities),
- the average business mix is approximately 58 percent contract testing and 42 percent in-house testing although many laboratories do only contract or only in-house testing,
- the average employment is 57 persons per laboratory and an estimated 16,000 employees constitute the industry's total labor force,
- the labor force is composed of 36 percent professionals, 45 percent technicians, 13 percent managers and administrators, and 6 percent other staff,
- measurable industry concentration exists but it is not enough to restrict market entry or control key resources,
- current annual sales are about $650 million or $2.3 million per laboratory, and
- the industry has an average testing space of 28,100 square feet per laboratory.

Toxicological testing can be divided into four general areas: mammalian, in-vitro, environmental effects, and chemical fate testing. Most toxicology laboratories will also perform product and analytical testing (though the latter is generally not considered toxicological testing). The incidence and estimated volume of testing in these six areas is shown in Exhibit 1.

Mammalian testing, the largest general area of toxicological testing, includes several specific types of tests: acute, subchronic, chronic, reproduction, teratogenic, oncogenic, and histopathological. These may also contain additional sub-types of tests. Acute testing is the most common type of mammalian testing performed. The most commonly used mammals for testing are small rodents (mice, rats, gerbils, hamsters), and they are used in 97 percent of the mammalian laboratories with an average use or inventory of 11,000 per laboratory.

In-vitro testing categorizes those biological tests which are conducted outside the organism; environmental effects testing seeks to determine toxic effects on an entire aquatic or terrestrial ecological community; and chemical fate testing assesses the persistence or changes of a chemical substance in the environment. All of these are important testing areas; however, their testing volume is relatively low compared to that for mammalian testing, their resource constraints are not considered serious, and the impact of TSCA regulation on them will not be as great or as direct as it will be on mammalian testing.

The supply of toxicological testing is dependent on the industry's capacity. Currently, excess capacity exists in all major testing areas, and surveyed laboratories indicated they could perform about 20 percent more testing. That margin indicates an industry utilization rate of 80 to 85 percent--the result of recent declines in demand from that which was anticipated during the mid-and late-1970's.

The key resources used in supplying testing services are professional and technical manpower, animals, equipment, supplies, laboratory space, and capital. Currently, capital and professional manpower are the most constraining resources on industry expansion. Capital is understandably a cyclical constraint; however, the constraint imposed by a shortage of professional personnel can be of long term because of the lengthy period required for professional preparation. The availability of other resources is not as critical to expansion according to laboratory officials.

Demand for Toxicological Testing

The study characterizes toxicological testing demand both by alternative sources and by their key resource requirements. The study estimated regulatory, nonregulatory (commercial), research, and aggregate demand for toxicological testing and its key resources. Non-testing demand was found to compete significantly for manpower resources (particularly veterinary pathologists); however, the non-testing demand for other toxicological resources was not found to cause resource constraints.

Exhibit 1. Estimated number of U.S. toxicology laboratories and their volume of testing (dollars) by testing area, 1981

Testing area	Toxicology laboratories		Volume of testing			
			Total testing		Toxicological testing 1/	
	(%)	(No.)	(%)	($ mil.)	(%)	($mil.)
Mammalian	63	180	38	250	56	250
In-vitro	51	150	12	80	18	80
Environmental effects	51	150	13	80	18	80
Chemical fate	48	140	7	40	9	40
Product and analytical (toxic and non-toxic testing)	81	230	30	200	NA	NA
TOTAL			100	650	100	450

1/ Excludes product and analytical testing which may or may not be related to toxicological testing.

NA = Not Applicable

Source: Francke, 1981.

The study's primary methodological concern in estimating demand was to include all sources of demand; thus, for this analysis, demand was divided into three components--regulatory (derived from a particular agency or act), nonregulatory (private, commercial), and research.

Regulatory demand was defined as all testing required by the federal government under TSCA, FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act), and FFDCA (Federal Food, Drug and Cosmetic Act). Although direct data are not available to estimate such regulatory demand definitively, the following observations indicate the general magnitude of the task.

FIFRA requires health and safety testing in the registration of pesticides. In addition to overseeing new pesticide registration, EPA is required to reregister all currently registered pesticides--some 1,400 active ingredients and some 38,000 formulations. EPA will eventually review existing toxicological data on each pesticide to determine the testing requirements for reregistration. EPA estimated the testing demand for nineteen acute, subchronic and chronic tests under FIFRA for both new active ingredients and formulations and for those which will be reregistered, and estimated as well as the number of pesticides which will require such testing. There are a number of uncertainties associated with these estimates: uncertainty exists concerning the number of pesticides which will be affected or the rate at which EPA will require such testing. Estimates suggest that FIFRA's annual testing demand requires over 4,000 tests each for the categories of acute dermal and oral tests; over 3,000 each for acute inhalation, primary eye, and dermal irritation tests; 2,000 dermal sensitization tests; and fewer than twenty each for acute neurotoxicity, subchronic (oral, dermal, inhalation and neurotoxicity), chronic (feeding, oncogenicity, teratogenicity, reproduction and mutagenicity), and metabolism tests.

The study considered TSCA testing demand as required under the TSCA's Section 4 (the testing of existing chemicals as recommended by the Interagency Testing Committee (ITC)) and the TSCA's Section 5 (the testing associated with new chemicals). The study's projections of the number of chemicals, the types of tests, and the aggregate test demand under Section 4 requirements were based on EPA's first proposed test rules for seven chemicals or categories in 1980. Section 5 annual testing was projected on the basis of the test data presented in premanufacturing notices (PMN's) in 1980. Section 4 will require an annual volume of sixty tests each for the test categories of oncogenicity, mutagenicity, teratogencity and chronic effects; forty-five reproduction tests will be required. Approximately 200 tests each for the categories of acute oral, primary dermal, and eye irritation; approximately one hundred Ames and acute dermal, forty-eight dermal sensitization, thirty-one acute inhalation and sixty-five other tests may be done for new chemicals. (These estimates are dependent on several factors, i.e., EPA regulatory schedules and anticipated new chemical introductions by private industry).

FFDCA requires manufacturers to document the safety of human and animal drugs, food additives, and cosmetics. Historical data exist for the testing of human drugs, and based on these data, the number and kind of tests and chemicals tested annually were derived. An estimated 3,000 acute oral tests will be required, as well as 300-600 subchronic oral tests; 130-180 each for acute dermal, inhalation, and dermal irritation tests; 86 primary eye irritation tests; and fewer than 50 dermal sensitization, subchronic oral 12-month, ophthalmic, and vaginal-rectal application tests.

Animal drug registration requirements initiate an approval procedure similar to that for human drugs. Except for teratology tests (approximately 164), fewer than 100 acute toxicity, skin or eye irritation, subacute, chronic and multigenerational reproduction tests will be generated annually under animal drug approval requirements.

Food additive testing, in addition to abiding by the above germane requirements, is responsive to FDA guidelines. The number of 1980 additives, by type, submitted for approval, combined with the tests required for each type yielded this study's estimate of the toxicological testing for additives: acute oral toxicity tests--184; lifetime feeding studies, short-term feeding studies, and multi-generational reproduction feeding studies--141; and subchronic feeding studies--73.

Both research demand and commercial (private) demand, the latter considered substantial, also contribute to total annual toxicological demand. Research demand is difficult to estimate, but government sponsored research includes that generated by the $69 million budgeted for the National Toxicology Program in FY 1980.

In summary, TSCA, FIFRA and FFDCA demand, and nonregulatory demand, must be aggregated and categorized into specific resource requirements. Estimates of the resources consumed by each test are necessary to this conversion of demand into resource units. Such estimates were available for some tests, and this study estimated the aggregate demand for one resource--board-certified veterinary pathologists: 475 veterinary pathologists, of a total of 486 available in 1980, could be utilized by combined TSCA, FIFRA and FFDCA toxicology testing demand.

Conceptual Supply-Demand Model Development

In its concluding chapter, this study also presents a conceptual supply-demand model of the chemical testing industry (toxicological testing only) and illustrates its implementation with a specific example. The formulation of the model indicated that substantially more quantitative supply, capacity, and demand data are needed to effectively implement the proposed model.

The concluding chapter presents, then, a general analytical system for characterizing the economic profile of the chemical testing industry. Besides including traditional supply and demand modules in the economic system, the system outlines three related modules that are needed for a dynamic analytic model: capacity, growth, and price-profit response. Only the capacity module is developed in detail in conjunction with the supply and demand modules.

The supply and demand modules of the model are explicitly defined for the toxicological testing industry. Both supply and demand are expressed in common resource units, i.e., key resources that are potentially constraints over the industry. Because the toxicological testing industry is essentially a service industry, the capacity (and supply) of the industry's laboratories should be determined by their capabilities and resources rather than by any pre-defined unit of testing. Additionally, to reflect the unique characteristics of the industry's multiple supply sources (e.g., independent and captive laboratories) and multiple demand sources (e.g., regulatory agencies and Acts and other), the model, as presented, incorporates two separate, but linked, subsystems: an accounting subsystem and an economic subsystem. The accounting subsystem is designed to track resource-specific components of the model and to establish accounting-type conditions. The economic subsystem focuses on economic conditions and constraints as reflected through simulated supply and demand functions and optimization criteria.

Overall the proposed model is presented as a mathematically programmable, simulation system, i.e., one that is effectively a multi-equation system. The model discussion concludes with a summary of the research implications of this study's conceptual model development and the data needs for implementing the model. Much of the needed supply-related data for the model are obtainable from this study's toxicology laboratory survey or proposed extensions of it which would add resource-specific and growth-related data. The needed demand data are also partially developed in this study, although a much larger research effort is necessary to adequately characterize toxicological testing demand for existing and newly developed chemicals. Each chemical substance tested may require various toxicological tests with differing protocols that involve many testing resources.

While a modeling approach appears technically feasible, it will require substantial additional research. In the near future, periodic surveys may be adequate to characterize changes in the toxicological testing segment of the chemical testing industry. From these, the industry's changing capacity and utilization can be estimated; the reasonably foreseeable availability of resources to perform additional toxicological testing can also be estimated. Projecting the expected level of aggregate testing demand arising from both private and regulatory sources will be the major remaining analytical issue.

I. INTRODUCTION

A. Background

Section 4 of the Toxic Substances Control Act (TSCA) authorizes the Administrator of the Environmental Protection Agency (EPA) to develop health and environmental effects data on chemical substances which may present unreasonable risks to either health or the environment. In promulgating such rules, the Administrator is required, under Subsection 4(b) (1), to also consider:

> ". . . the reasonably foreseeable availability of the facilities and personnel needed to perform the testing required under the rule."

For the Administrator to forward the development of the regulations and guidelines required, the available capacity of the chemical testing industry to perform the tests required within reasonable time limits must be determined.

The potential magnitude of TSCA testing efforts is indicated by the fact that there are 55,000 chemicals on the TSCA inventory of chemical substances. Although not all chemicals will be subject to Section 4 testing requirements, the volume of testing potentially required by TSCA poses questions concerning the adequacy of the existing capacity of the chemical testing industry.

Other chemicals are also likely to be tested because of TSCA, and the testing requirements are expected to increase in terms of the types, numbers, complexity and duration of tests. Other regulatory programs requiring comparable testing may result in yet additional testing demands; consequently, to be most accurate, TSCA-related testing demands should be assessed within this broader demand framework.

As the chemical toxicological testing industry has expanded to meet these anticipated demands upon its resources, two consequential factors have become clear. In the first instance, predicted demand increases have not been fully realized; hence, the industry has but partially expanded. And in the second instance, though apparently most supply resources appear adequate to demand, capital constraints and a shortage of qualified professional and technical personnel limits the industry's present capabilities and capacities.

Based on an examination of chemical testing literature, the industry can be grouped into three major categories: (1) biological chemistry testing, (2) environmental chemistry testing, and (3) product chemistry testing (See: Exhibit I-1). For the most part, toxicology testing encompasses the first two categories of chemical testing, biological and environmental. Biological chemistry testing--a major focus of this study--can also be further categorized into acute, subchronic and chronic testing.

Acute toxicity studies are used to evaluate the short-term effects of a given chemical or drug and they provide the basis for later, more comprehensive tests. The simplest acute toxicity test is an LD50 test, one which determines the dose that would be lethal to 50 percent of a representative target animal population.

Subchronic toxicity studies provide data on the toxic effects of a chemical and determine the dose level and time required for these effects to be produced. Dosing duration is generally between thirty to ninety days, periods during which time clinical, biochemical and pathological evaluations are initiated. Subchronic studies aid in discerning the potential toxic effects of repeated chemical dosages.

Chronic toxicity studies are generally performed for periods varying from six months to the lifetime of the test animal. These studies assess the long-term reproductive, genetic, teratogenic, oncogenic, and carcinogenic effects of long-term exposure to a chemical. The state of the art is such that no one comprehensive test adequately evaluates all potential mutagenic effects. Consequently, most laboratories conduct a series of in vitro (outside living organism) and in vivo (inside living organism) studies.

B. Scope of the Analysis

The two main objectives of the study were:

- to develop an economic profile of the chemical testing industry, and
- to prepare a comprehensive listing of chemical testing laboratories.

To forward these objectives, the study considered industry data to provide the following information and to include it within this report.

-----The availability of testing services and the adequacy of the chemical testing industry to meet regulatory-related demands were examined. In particular, the supply of key resources--manpower, space, animals, equipment, supplies and capital--required to conduct quality testing were assessed via a survey. Particular emphasis was given to the biological chemistry testing segment. The industry's possible constraints on growth were also examined.

Exhibit I-1. Major segments of the chemical testing industry and associated types of tests. 1/

Biological (Animal) Chemistry

Acute Testing

Acute oral toxicity
Acute dermal toxicity
Acute inhalation toxicity
Primary eye irritation
Primary dermal irritation
Dermal sensitization
Acute delayed neurotoxicity
In vitro genetics

Subchronic Testing

Subchronic oral dosing
Subchronic 21-day dermal toxicity
Subchronic 90-day dermal toxicity
Subchronic inhalation toxicity
Subchronic neurotoxicity
In vivo genetics
Teratogenic
One generation reproduction

Chronic Testing

Chronic feeding study
Oncogenicity studies
Teratogenicity studies
Long-term reproduction studies
Carcinogenicity studies
Multigeneration genetic studies
Multigeneration genetic reproduction

Environmental Chemistry

Physio - chemical Degradation 2/

Chemical transformation: hydrolysis
Chemical degradation: oxidation
Photochemical transformation in water

Metabolism

Aerobic soil
Anaerobic soil
Anaerobic aquatic
Microbes on chemicals
Chemicals on microbes
Activated sludge

Mobility

Leaching
Volatility
Adsorption
Water dispersal

Field Dissipation

Soil
Water
Ecosystem

Ecological Effects 3/

Cellulose decomposition
Nitrogen transformation
Sulfur transformation
Microbial effects tests
Plant effects tests
Animal effects tests
Algal inhibition test
Lemna inhibition test
Seed germination and early growth

Accumulation

Special Chemistry

Product Chemistry

General Physical/Chemical Properties

Water solubility
Vapor pressure
Adsorption
Boiling/melting/sublimation points
Density/specific gravity
Dissociation constant
Flammability/explodability
Particle size
pH measurement
Chemical incompatibility
Vapor phase UV spectrum for halocarbons
Ultraviolet and visible absorption spectra in aqueous solution

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1/ Preliminary. Additional tests may be applicable within each segment.
2/ Includes product chemistry types of testing.
3/ Includes biological chemistry types of testing, e.g., animal effects.

-----The total demand for chemical testing services--regulatory, non-regulatory and research--and the incremental demand for testing generated by Section 4 TSCA were assessed. In addition to these demands, the non-testing demand for testing resources was estimated in order to fully characterize the market for toxicological testing.

-----Finally, a conceptual supply-demand model of the chemical testing industry was constructed to provide a predictive tool for assessing future industry trends when the required detailed data become available.

-----A list of laboratories capable of performing the type of testing required under Section 4 TSCA was compiled from information assembled in the course of the survey. This listing, an integral part of the chemical testing supply section of the study, is included in Appendix A.

C. General Approach

Initially, literature and data reviews were conducted. The resultant toxicology testing information is summarized in Chapter II of this report and provided selected material for subsequent chapters on supply and demand.

The study's literature review also identified data shortages characteristic of chemical testing supply and demand. Chemical testing supply was partially characterized in this study by a number of lists of laboratories/facilities which conduct toxicology testing and by a partial documentation of key personnel resources, i.e., certified pathologists, toxicologists, and technicians. However, the laboratory data sources used for such characterization were found to be inadequate in several respects: they were often out-of-date, non-descriptive, and usually limited to the laboratory name and address (often incomplete). Accessible chemical testing demand data sources primarily reflect direct government demand. Private testing demand and the distinction between government-induced and voluntary testing demand were not found in existing data and hence, these demands could not be assessed independently, from information in current literature.

The industry structure was defined and characterized from secondary sources and discussions with industry representatives, and telephone survey interviews of laboratories. From the survey of toxicology testing laboratories, the testing capabilities, capacity and utilization of capacity were assessed. The survey also helped identify and evaluate resource constraints. The toxicology testing industry and supply characteristics are discussed in Chapter III. The list of chemical testing laboratories, included in Appendix A, contains independent commercial laboratories, captive laboratories and selected private research and university laboratories.

In Chapter IV, the sources of industry demand are evaluated. These include U.S. government regulatory agencies and research institutes, private industry, private foundations, and universities. Although much of the demand for toxicological testing is directly or indirectly generated by federal regulations, data from written records and information supplied by regulatory agencies' personnel indicate that the amount of testing demand generated by regulation, in a particular year, is extremely difficult to estimate. Specifically, short delays in issuing regulations and budgetary fluctuations result in actual demand volumes that can differ enormously from predictions made six months before. Demand projections, therefore, must be made by examining the projected development of the regulatory programs over the next several years, rather than by examining plans for a single year.

In order to characterize fully the market for toxicological testing, the non-regulatory generated demands for testing resources must not be neglected. This study's information gathered from professional associations permitted an estimate of these and, finally, the existence of a non-testing demand for toxicology testing resources is acknowledged, no estimates were made of its magnitude.

Chapter V presents and discusses a conceptual supply-demand model of the industry within a systems analysis framework. This model is resource based and is segmented by testing categories. Although the complete supply-demand data required for implementing the model and for using the model for predictive purposes are not available, its conceptual developments are documented so that later model implementation may be more readily accomplished when data are sufficient. The research implications of the study, the data needs, and the possible methods of acquiring such data are summarized, also.

The list of toxicology laboratories is presented in Appendix A. The survey instrument designed and utilized to obtain more detailed toxicology laboratory information is included as Appendix B.

II. LITERATURE AND DATA REVIEW

Thorough analysis of the chemical testing industry requires that the economic characteristics of the industry and its markets be determined. To provide the framework for that characterization and to identify the data available for assessing the industry's baseline supply and demand for chemical testing services, this study initially reviewed germane literature and industry data sources.

A. Industry Structure and Organization

After assessing existing documents, journal articles, industry profiles and after consulting with industry and academic personnel, this study's researchers divided the chemical testing industry into three segments:

- Biological chemistry (mammalian, in-vitro, fish and wildlife)
- Environmental chemistry
- Product chemistry

Furthermore, each of these three segments was subdivided according to the types of tests each performs (See: Exhibit I-1). (These test subcategories will be discussed later in terms of their required resources.)

The rationale for dividing the market into three segments reflects both academic principles and industrial procedures. Biological (animal) chemistry testing encompasses a series of related tests. Specific tests are classified by genre (acute, subchronic, and chronic) rather than by target animal; consequently, an acute toxicity to fish test will be listed as a biological test and not a fish or wildlife test because it is categorically an acute toxicity test that incidentally uses fish as its target species.

Environmental chemistry testing includes physio-chemical degradation analysis, field dissipation assessment, and various ecological effects analyses. Resource competition between environmental chemistry and biological chemistry appears minimal due to the contrasting nature of the differing professional personnel, test procedures, and testing equipment required to conduct the various tests in each test category. Such separation makes market segmentation both applicable and desirable for the purposes of the present industry economic analysis.

Product chemistry is that category which focuses on determining general physical and chemical properties (e.g., vapor pressure and absorption). A wide variety of analytical laboratories can perform these tests and their personnel and other resource requirements appear to compete but minimally with the two other categories. The economic characteristics of the product chemistry industry, then, may also be assessed separately. Additionally, product chemistry is not conceptually included among those technologies more directly involved with health and environmental effects testing--although TSCA may require such testing data.

The primary focus of this study is on the biological chemistry segment of the chemical testing industry. Expected to have the most critical personnel and other resource constraints, this segment is that which will be most affected by the expected testing requirements of Section 4 of TSCA.

B. Literature/Data Review

Because chemical testing capacity has only recently become an important underlying issue in the development of federal policy on the regulation of chemicals, relevant literature is sparse. The literature reviewed for the present study consists of several periodical articles and two recently completed reports for EPA. This literature is briefly summarized below.

1. Profile of the Chemical Safety Testing Industry: An Assessment of Pesticide Testing Capacity (May 1980)

This profile study, completed by ICF for the EPA's Office of Pesticide Programs, addresses the ability of the chemical testing industry to meet those demands stemming from the generic approach to pesticide registration. The approach used in the study was:

- to determine those segments of the market in which constraints to supply do or potentially exist, and
- to compare total projected demand with total projected supply for those segments with supply constraints.

Because the chemical testing industry is not well documented, the profile employed data gathered from a variety of sources including:

- personal and telephone contacts with representatives of government, trade associations, and laboratories,
- available documented sources (See: "References" at the end of this report), and
- a written questionnaire completed by fifteen laboratories.

Within the limits of the information obtained, the ICF's profile made implicit the following observations and implications that are consequential to the present study:

Observation 1 - The supply of high-quality animal testing is constrained primarily by the supply of veterinary pathologists and, to a lesser extent, by the supply of toxicologists. Other resources, such as laboratory space, capital, and equipment, are also potential short-term constraints.

Implication: The availability of adequately trained professional manpower is clearly an important determinant of the supply of toxicological testing services and should be a major focus of supply assessment.

Observation 2 - Large variations in reported testing prices for reasonably well defined protocols suggest that testing laboratories compete on factors other than price.

Implications: Because this is a market for services rather than commodity goods, decision modeling based solely on price will not adequately reflect market behavior.

Observation 3 - Current research in genetic toxicology may result in significant breakthroughs in testing technology, breakthroughs that potentially change the testing resources currently necessary to meet toxicological testing demand.

Implications: A supply-demand model must be so designed with sufficient flexibility that it can accommodate changes in testing technology.

2. Cost Analysis Methodology and Protocol Estimates: TSCA Health Standards and FIFRA Guidelines (April 1980, draft report to EPA)

Enviro Control Incorporated and Borriston Laboratories completed this draft report for the Office of Regulatory Analysis (currently Regulatory Impacts Branch) of EPA's Office of Toxic Substances. The study developed a methodology for estimating the cost of health effects testing protocols. Pricing determinations applicable to protocols for several acute, subchronic, chronic and mutagenic tests were made directly by Borriston Laboratories and by a limited survey (less than 10 contacts) of other testing laboratories. Results indicated that price estimates for a well defined protocol can vary by as much as plus or minus 50 percent from the average.

In providing price estimates, Borriston characterized each protocol in terms of the component resources it utilized. If these resources' breakdowns are sufficiently validated, they can serve as useful inputs to the implementation of an industry supply model. Because the survey showed broad ranges for price data, the report is a further indication that the industry competes on factors other than price. A supply model design, therefore, should separate the industry's physical resources and requirements from its associated cost and price data in determining the industry's supply-demand specifications.

3. Other Literature

A variety of other literature sources such as toxicology laboratory directories, technical and industrial journals, and various federal publications provided evidence of the following concerning the chemical toxicological testing industry.

- Capacity--There is a potential shortage of overall health and environmental effects testing capacity. (Anon., 1980a; Murray, 1978; West, 1979.)

- Manpower--There is a shortage of qualified professional personnel underlying the industry's potential capacity shortage. (Abelson, 1978; Anon., 1978b; Keller, 1979; Maugh, 1978; Murray, 1978.)

- New Technology--Mutagenicity testing is a growing area of toxicological testing and has the potential to redefine the market for such testing. (Anon., 1980b; Haworth, 1979; Maugh, 1979.)

- Quality--Testing firm reputation and other non-price factors are important for both facilities and personnel. (Anon., 1980a; Keller, 1979; Murray, 1978; West, 1979.)

- Laboratory Classification - Chemical testing laboratories can be classified into three general groups:

  - Commercial
    - independent
    - captive
  - University
  - Government

The present study so classifies the industry in order to analyze its sources of chemical testing resources and to identify and compile a list of chemical testing laboratories.

C. Data Sources and Limitations

Historically, the chemical testing industry has not been well documented as an economic sector; consequently, no regular statistical reports exist on the structure and performance of any segment of this industry. This section of this report does, however, briefly summarizes a number of data sources that are germane to estimating industry resource supply and industry demand.

1. Data Sources: Supply

Relevant supply data include partial information on laboratories, personnel, and other resources. Several lists of selected laboratories are available, as shown in Exhibit II-1. With some exceptions, these lists present problems to the researcher.

- Most are not compiled or updated regularly; rather, they are one-time efforts (except those of the American Council of Independent Laboratories).
- They do not sufficiently describe the testing services offered (except those of the Society of Toxicology).
- The resources that affect supply capacity are not well documented.
- The validity of descriptive information, when provided, is unknown.

Nevertheless, these lists provided the foundation for a master list of laboratories which provide chemical testing services. This preliminary list was used initially as a source of contacts for a telephone survey of laboratories conducted to identify their services and characteristics. (Francke, 1981.)

A few documented data sources are available which discuss the industry's professional manpower. The American College of Veterinary Pathology publishes data on the number and the activities of board-certified veterinary pathologists, but few other data are available. Information on other pathologists (M.D., Ph.D., D.O., D.D., other D.V.M.) may exist from other trade associations; however, the extent to which these other pathologists would be considered "qualified" under the final TSCA testing guidelines is unclear. The National Institute of Environmental Health Services (NIEHS) has proposed a study germane to toxicological manpower needs. The study will develop a taxonomy that will classify toxicologists and toxicology training programs and will be instrumental in projecting the supply of future toxicologists. In addition, some certifying organizations exist for technicians (histology technicians and animal handling technicians). These organizations could provide basic information about the supply of such technicians.

Information on the supply of other resources, such as animals and equipment, must be obtained directly from suppliers.

2. Data Sources: Demand

The present study also assessed to the extent possible both government-related and private demand. The former includes both regulatory and direct research demands; private demand includes that industry testing for product development and evaluation which is not directly attributed to regulation. (Private research includes also, the demands made upon university and foundation research efforts.)

Exhibit II-1. Partial source listing of testing laboratories, chemical testing industry study

1. EPA, Office of Pesticide Programs, June 1977.

   List of 381 laboratories which was cited as a source of data in support of a registration application for pesticides, 1947-77. List also notes how many times each lab was cited as a source.

2. Food and Drug Administration (List of laboratories that have performed work submitted to the FDA), June 1979.

   This list of about 500 labs contains information about the type of laboratory (government, sponsor, contract, or university) and the Bureau within FDA where data were submitted, June 30, 1979.

3. American Council of Independent Laboratories, Inc., Directory 1978.

   About 200 member laboratories give descriptions of their service in this directory which is indexed by geographical location and type of service performed. Most of these laboratories offer primarily analytical chemistry and chemical engineering services rather than toxicological testing.

4. Society of Toxicology, Toxicology Laboratory Survey, March 1976.

   This booklet on about 130 laboratories is based on a mailed survey of all members of the Society of Toxicology. Information on each lab includes the type of tests performed, in-house capabilities and personnel, experience with types of compounds, and whether lab does contract work.

5. Chemical Times and Trends, "Testing Laboratory Directory", Oct. 1979.

   About 120 laboratories that perform toxicological testing are listed in this issue of the Journal of the Chemical Specialties Manufacturers Association. Addresses, phone numbers, names of contracts are provided and whether the laboratory is currently accepting contracts.

6. Tox-Tips (Toxicology Testing in Progress), National Library of Medicine, December 1979.

   This monthly bulletin prints an index of institutions and investigators in its quarterly issues for all studies participating in the project.

7. Mutagenicity Testing Laboratories in the U.S. Compiled by Dr. Michael D. Shelby, Office of the Associate Director for Genetics, National Institute of Environmental Health Sciences, November 1979.

   This booklet contains names and addresses of 43 laboratories that perform mutagenicity tests and lists the specific tests available or under development at each laboratory. Also indexed by geographical location and type of test.

8. "Report of the Subcommittee on Inhalation Toxicology of the Department of Health Education and Welfare Committee to Coordinate Toxicology and Related Programs", Raymond E. Shapiro, Executive Secretary, Journal of Environmental Pathology and Toxicology, 1:353-381, November 1977.

   Contains a list of 15 academic institutions, 16 government facilities and 39 private labs that perform inhalation toxicology testing. Describes present facilities in each lab, studies being done, capacity, and future plans.

9. National Association of Life Science Industries, Membership List, May 1978.

   List of 21 members of NALSI and names of laboratory representatives to the association.

10. American Society for Testing & Materials. Directory of Testing Laboratories. 1975.

    Approximately 90 of the 439 laboratories in this directory are listed as having toxicological capabilities. All are equipped to undertake testing on a fee basis. Specific tests, staff, capacity and experience are not recorded.

11. Analytical Chemistry, "Laboratory Guide Issue", August 1979.

    This annual guide includes an alphabetical list of analytical and research services.

12. Thomas Register of American Manufacturers, 1980

    Numerous listings of laboratories are presented in "environmental", "experimental" and "research and testing" categories. Besides address and phone numbers, Thomas includes a very brief indication of type of service, a classification by "approximate minimum tangible assets", and, for some laboratories, either an advertisement or reproduction of the company catalog.

13. DHEW, Toxicology Research Projects Directory.

    This monthly directory of projects classified by toxic agent, research orientation and areas of environmental concern includes a subject index and a performing organization index (cumulated annually). The sponsoring and performing agencies both include a variety of government and non-government institutions.

14. Industrial Research Laboratories of the United States, 1977 Bowker 15th Ed.

    Most of these research facilities are owned and operated by industrial firms, foundation-supported facilities and university labs independent of university control. In addition to addresses and phone numbers, the directory includes names of principal executives, number of professional staff, a fairly specific statement of research and development activity and whether facilities are available for non-company projects. Over 120 laboratories are listed as conducting toxicological testing.

Source: Compiled by ICF Incorporated and Development Planning and Research Associates, Inc.

There is little documented information available which can be used to readily and accurately determine the demand for chemical testing. The following programs (other than TSCA) appear significant in their effect on creating industry demand.

- Federal Insecticide Fungicide and Rodenticide Act (FIFRA)
- Food and Drug Act (FDA)
- National Institute of Environmental Health Services (NIEHS)
- National Institute for Occupational Safety and Health (NIOSH)
- National Cancer Institute (NCI)

This study's efforts to identify demand data did result in the following general observations concerning the characteristics and availability of demand data sources.

Estimates of the testing demand generated by government-related programs are usually subjective ones made by appropriate government personnel. However, they are often reluctant to have their appraisals used for analytical purposes.

The estimates on testing consequent to government-supported research are more objective. Most research agencies maintain documented plans for and lists of on-going projects which can be used to estimate this component of demand. Such documentation exists for NIOSH, NCI and for the National Toxicology Program in general. EPA and FDA research-generated demands are generally documented. Finally, some developmental work with new chemicals subject to pre-manufacturing regulation under Section 5 of TSCA can be documented.

Private (non-statutory responsive) demand both in general and specifically for product development and evaluation were neither found nor identified.

Existing data do not clearly distinguish between regulatory-induced demand and voluntary demand. In developing this study's baseline demand, such a distinction, however, is not necessary, for both regulation-induced and voluntary testing should be included and aggregate resource demand identified. The relevant information required for an assessment of TSCA induced changes in the baseline demand are (1) the classes of chemicals for which testing is required, (2) the types of tests that may be required, and (3) the probability of the tests being performed. Impact and sensitivity analyses could show how future patterns of regulation or research could change the baseline demand.

III. THE TOXICOLOGICAL TESTING INDUSTRY AND SUPPLY OF TESTING RESOURCES

The toxicological testing industry's supply is clearly dependent upon the availability of its critical resources: manpower, laboratory space, animals, equipment and capital. Skilled toxicologists capable of designing and performing studies, especially those in biological testing, are critical to the industry. Pathologists are needed, as well, to examine tissues consequent to those studies. Laboratory space, a potentially constraining resource, is critical to the industry for it is one in which varied tests and studies must be conducted concurrently and in distinctly separate testing areas and individual animal rooms. Laboratory animals, especially those resulting from unique breeding and specific species requirements, are a potential constraint of long-term significance. Highly automated, precision equipment is required so that varied, reliable, and reproducible test data may be obtained by the industry. Finally, industry capital availability is significant, so that the necessary quality and quantity of such critical resources can be maintained.

This chapter assesses the supply of toxicological testing and the industry's ability to meet the demands exercised by public and private entities. Much of the information presented reflects that of a recent survey (Francke, 1981) of the chemical testing industry, a survey which identified toxicology testing laboratories and their characteristics and capabilities. This survey's data are supplemented by information from other research literature, industry publications, and from contacts with industry technical and administrative personnel.

The chapter is organized in four parts:

A. Profile of the toxicological testing industry--a background discussion of the industry which includes its number of firms, employment, sales, concentration and other general characteristics.

B. Testing capabilities - a discussion of the toxicology testing performed by laboratories.

C. Capacity and utilization - a discussion of the industry's capacity and ability to increase testing.

D. Resources supply and constraints - a discussion of the adequacy of the industry's professional manpower, test animals, laboratory space, capital, and other critical resources.

A. Profile of the Toxicological Testing Industry

The former Division of Chemistry of the United States Department of Agriculture conducted toxicity testing as early as 1880; however, not until passage of the 1938 amendments to the Federal Food, Drug, and Cosmetic Act of 1906 did government regulation begin to generate substantial toxicology testing. Prior to these amendments, small-scale, in-house testing was carried out by some of the chemical and pharmaceutical producers. The 1938 amendments required producers to submit proof of the safety and effectiveness of their products prior to marketing. Although this legislation did not include specific testing requirements, its effect was to initiate testing on a large-scale basis and prepare the way for the growth in independent laboratories and the expansion of in-house facilities which occurred during the 1970's. (Anon. 1980c; Veraska, 1980.)

1. Number of Laboratories

Toxicology testing has recently become a major business in the United States. Much of the industry's growth was in response to the demand stemming from such federal statutes as the Toxic Substances Control Act (TSCA) of 1976, and the amendments to the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). Although the Resource Conservation and Recovery Act (RCRA) and the Clean Water Act (CWA) do not specifically require testing, their provisions also furthered the growth of testing. As now written, these and similar laws will continue to generate demand for toxicology testing, and the industry should sustain long-term growth.

While toxicology testing is a major industry, its relative newness has prevented the development of a comprehensive information base from which to profile it. This limitation has been alleviated significantly by a recent survey which contacted about 800 laboratories to determine if they qualify as toxicological testing laboratories. 1/ The survey identified 272 laboratories that perform toxicological testing, and of these, 242 cooperated and responded to the complete survey while 30 did not. 2/

The survey depended on public listings and referrals for its initial screening list of 800 chemical laboratories. The various public listings used spanned the last six years, and none was comprehensive. These limitations plus the time constraints and some refusals prevented complete industry coverage, as intended, and the end result was a large sample survey.

1/ The survey was done as a supplement to this present analytic report of the toxicology industry and was carried out jointly for the Environmental Protection Agency by Development Planning and Research Associates of Manhattan, Kansas, the Center for Public Affairs of the University of Kansas, and ICF Incorporated of Washington, D.C. The survey, approved by the Office of Management and Budget (OMB No. 2000-0141), constitutes Appendix B of the present study.

2/ A listing of all laboratories which indicated they performed toxicological testing is included in Appendix A.

Nevertheless, its coverage is extensive and the 242 responding firms are a significant proportion of the estimated 280 to 290 existing toxicology testing laboratories. This report, then, uses an industry population estimate of 285 toxicology laboratories for its descriptive and analytic characterizations of the industry.

2. Employment

The survey responses of the toxicology laboratory personnel indicated that the industry employed an average of 57 employees per laboratory in 1980 or a total of slightly more than 16,000 (57 x 285 firms). The relative distribution of this employment among professionals, technicians, managers and administrators, and other staff is:

	Percent of employees	Number 1/
Professionals	36	5,800
Technicians	45	7,200
Management & Administrative	13	2,000
Other Staff	6	1,000
Total	100	16,000

Large variations exist among laboratories regarding employment, with sizes ranging from five or fewer employees to over five hundred. Overall, the following distribution by size is estimated:

Number of employees per laboratory	Percent of laboratories
1-10	28
11-50	48
51-100	13
101 or more	11
	100

3. Laboratory Space

Laboratory space is another critical resource affecting the industry's capacity for toxicological testing. Test conditions can require extensive animal cage space as well as inhalation chambers that are especially dependent upon restricted, specialized areas.

The surveyed toxicology laboratories contained an average of 28,100 square feet. Again, substantial variation exists within the industry--many small laboratories contain fewer than 5,000 square feet and the very large, over 100,000 square feet. The distribution of laboratories by general size categories is:

1/ Estimated to nearest two significant digits.

Square feet of laboratory space	Percent of laboratories
5,000 or less	40
6,000 to 20,000	31
21,000 or more	29
	100

Much of this space is apparently new, for considerable laboratory space expansion has occurred in recent years. A review of industry literature and conversations with industry officials provide the following examples of new expansion in laboratories.

- Mobay and Stauffer recently completed 60,000 square foot animal test facilities. (Chemical Marketing Reporter (CMR), 11/05/79, p. 16; Chemical Week, 1/23/80, p. 38.)
- In 1978, Goodyear Tire and Rubber Company added a $100,000 testing laboratory to its existing research facilities in order to investigate whether new tire industry chemicals are hazardous to human health. (Chemical Marketing Reporter, 9/11/78, p. 32.)
- In April, 1980, ICI Americas, Inc. applied for a $43.5 million industrial revenue bond issue to finance a proposed expansion of the company's biological research center at Goldsboro, NC. (Wall Street Journal, 4/4/80, p. 19.)
- In January, 1980, Dow Chemical Company was in the process of adding 28,000 square feet to its toxicology testing laboratory at Midland, MI. The company has expanded this facility five times since its founding and it now employs sixty scientists. (Chemical Week, 1/23/80, p. 38.)
- Shell completed a 60,000 square foot toxicological testing laboratory at its Houston research complex during 1979 (Chemical Week, 1/23/80, p. 38.)
- During 1980, Allied, Monsanto and DuPont's Haskell Laboratories proposed additions to or were expanding their toxicology testing laboratories that had been completed just a few years previously. (Chemical Week, 1/23/80, p. 38; CMR, 10/9/78, p. 50; J. Commerce, 9/17/79, p. 50.)
  - In April, 1979, Allied completed a $1.4 million, 17,000 square foot animal laboratory. Another 25,000 square foot laboratory has been requested from the Board.
  - Monsanto plans to add to its 47,000 square foot, $12 million toxicology testing laboratory that was dedicated in the fall of 1978. Until completion of the present facility, Monsanto

had used independent laboratories to do safety testing, but according to a company spokesman, the company's research needs "outstripped the capabilities of these outside laboratories."

  - Haskell Laboratories completed a 70 percent expansion in 1976 and is now adding an $8 million facility which will further expand capacity by 30 percent.

- The Chemical Industry Institute of Toxicology completed a $10 million testing and research laboratory in Research Triangle Park, NC (CMR, 1/3/77, p. 7 and 6/20/77, p. 20.)
- In 1978, Medtronics, Inc. of Minneapolis, the world's largest manufacturer of cardiac pacers, opened an in-house toxicology laboratory for testing the chemical industry's products. The firm has extensive experience in testing its own products. (Chemical Week, 2/20/79, p. 48.)
- Syracuse Research Corporation completed an aquatic toxicology laboratory in 1979 to help the chemical industry meet new federal testing requirements. (Chemical Week, 2/28/79, p. 48.)
- Biospherics, Inc. of Rockville, MD, expanded its laboratory which monitors the effects of potentially toxic chemicals, pesticides, and drugs on aquatic animals and plants. (Environmental Science and Technology, 9/79, p. 1182.)
- Jacobs Engineering Group established a 12,000 square foot analytical laboratory at Pasadena, CA, in 1978. (Environmental Science and Technology, 8/79, p. 1089.)
- Litton Bionetics opened an 88,000 square foot laboratory in Rockville, MD, in 1978 to perform biological safety evaluation. (Graham, 1980.)
- International Research and Development Corporation completed a 100,000 square foot facility during the latter half of its 1978 fiscal year. (SEC, 1979) This addition, not fully utilized at the end of fiscal year 1979, has been contributing to the firm's increased costs and lower profits during the past few years.
- Hazleton Laboratories plan to begin work in the near future on a $10 million laboratory in Sterling, VA, where the company currently has a 103,000 square foot laboratory. (Rowe, 1981.)

4. Financial characteristics

Limited data are available on the financial characteristics of the toxicology laboratory industry. Three major factors contribute to this condition:

- The toxicology testing industry is but one segment of the chemical testing industry, and it has not been traditionally identified uniquely enough to have its financial characteristics reported separately.

- The toxicology testing industry is relatively young and dynamic, and historical data bases have not been established.

- Many laboratories are relatively small, private operations for which public information is not available.

Because of these conditions, information on financial characteristics are restricted to general estimates of industry revenue or volume of business and a small sample of data on service fees. No significant data were found on costs, operating margins, and capital structure.

The survey did not request information concerning the responding firms' specific financial characteristics. Such information is not critical to the assessment of testing capabilities, and traditionally it is an area in which low and unreliable response rates are experienced. However, a combination of the survey information and company financial reports and brochures does yield acceptable estimates of revenues. Specifically, a small sample of company brochures and reports shows that laboratories generate average annual revenues of $40,700 per employee. Applying this revenue factor to an industry employment level of 16,000 employees results in estimated industry annual revenues of $650 million or an average of $2.3 million per laboratory for 1981. This estimate approximates that quoted in a 1980 New York Times article which indicated that chemical testing by commercial laboratories had become a $500 million a year business. (DeWitt, 1980.)

Historical estimates on revenues are unavailable from the survey or published sources, but significant growth occurred through the 1970's, a growth primarily attributed to a perceived increased demand in response to environmental regulations and product liability related testing. In the last six to eighteen months that growth has slowed. If, however, such slowdown is due to the weakness in the nation's general economy and to uncertainty about key regulatory decisions that may be made regarding environmental issues (DeWitt, 1980; Veraska, 1980), such a slowdown may be temporary rather than a reflection of industry potential.

Company brochures and reports also provided a small sample of data on service fees for certain types of tests, primarily in the area of in-vitro and acute mammalian testing. These tests are relatively standard tests with more simple protocols and lower costs compared to chronic tests or environmental tests. As shown below, however, there is still a wide variation in service fees charged for comparable tests. The variation may reflect differences in testing quality, costs and cost accounting, marketing strategy, protocols and staffing.

Type of tests (sample size)	Range for service fees 1981 ($)
IN-VITRO	
Ames mutagenicity-plate and pre-incubation, duplicate (6)	375 - 1,200
Mouse lymphoma (4)	3,600 - 6,500
DNA repair - E. Coli polymerase assay (3)	300 - 575
Chromosome aberration (2)	3,500 - 4,000
Drosophila mutagenicity (2)	10,800 - 12,500
IN-VIVO	
Chromosome aberration-bone	
Rat (2)	13,500
Mouse (2)	10,000 - 10,800
ACUTE MAMMALIAN TESTS	
Oral-screening or single dose (8)	85 - 610
Oral - LD50 determination (6)	430 - 3,100
Dermal-screening or single dose (5)	240 - 1,100
Dermal - LD50 determination (4)	700 - 5,750
Primary eye irritation (6)	175 - 990
Primary dermal irritation (5)	205 - 660
Pyrogen-three rabbit-negative (5)	45 - 75

While these data are indicative of general price levels, they are insufficient in providing detailed information on average prices, price trends and relationships between testing supply and prices.

5. Concentration

Concentration in the toxicology testing industry can be estimated on the basis of the survey data related to employment by extrapolating that data through two measures of concentration: (1) a traditional concentration table which shows concentration ratios for sets of firms and (2) the more comprehensive "Lorenz curve." The latter measure shows, as a continuous function, the percentage of total industry employment level accounted for by the fractions of all firms ranked in order of size.

The following table shows employment concentration ratios for various sets of laboratories from the 235 firms that provided employment data.

Size of laboratories by employment (n = 235)	Percent of employment
Largest 4 (2% of sample)	17
Largest 8 (3%)	28
Largest 20 (9%)	48
Largest 50 (21%)	71
Smallest 100 (43%)	6
Smallest 200 (85%)	38

While these data do not include all laboratories, most of the largest are included and the small laboratories that are excluded represent a small percentage of total employment. Thus, these estimated concentration ratios are good estimators of actual levels (with but a small upward bias). The ratios indicate that the top four firms account for less than 20 percent of total employment. They could control slightly more of the industry's sales or testing (traditional measures of concentration) if these larger laboratories were to generate more sales or perform more tests per employee than do small firms. Large-firm market power, however, is still not expected to be dominant. Generally, 4-firm ratios in U.S. industries will range from less than five percent to over 90 percent with a ratio of less than 30 percent being considered relatively low.

Using the sample data and employing similar procedures of matching percent of firms ordered by size with percent of employment represented by these firms, a more comprehensive Lorenz curve can be developed to indicate concentration in the toxicology testing industry. The results of this procedure appear in Exhibit III-1. For example, the data indicate that the smallest 40 percent of the firms accounts for only 6 percent of the total employment--approximately 900 employees. This includes 114 firms employing 14 persons or fewer per laboratory. Moreover, the largest 20 percent of the firms (the 80 percent figure on horizontal axis) employs 69 percent of the employees of the industry (100% - 31%) or an estimated 10,350 persons. These are represented by firms employing 65 or more persons per laboratory.

In summary, employment data indicate that the toxicology testing industry exhibits a measurable amount of concentration, but the level is not high enough to restrict market competition or to allow individual firm control of key resources. Market power should also continue to be dispersed, for this is a growth industry which provides a relatively homogeneous, undifferentiated service with somewhat low capital requirements. Such characteristics traditionally stimulate competition and firm entry into an industry.

6. Type of Ownership

The ownership of toxicology laboratories providing commercial testing services is traditionally divided into two categories: captive (in-house) laboratories and independent (contract) laboratories. 1/ The latter are independently owned and operated and perform work for various clients only on a contract or bid basis.

Independent laboratories are organized either for profit or not-for-profit. Major not-for-profit laboratories include Battelle-Columbus Laboratories and Battelle-Pacific Northwest, Midwest Research Institute, and Stanford

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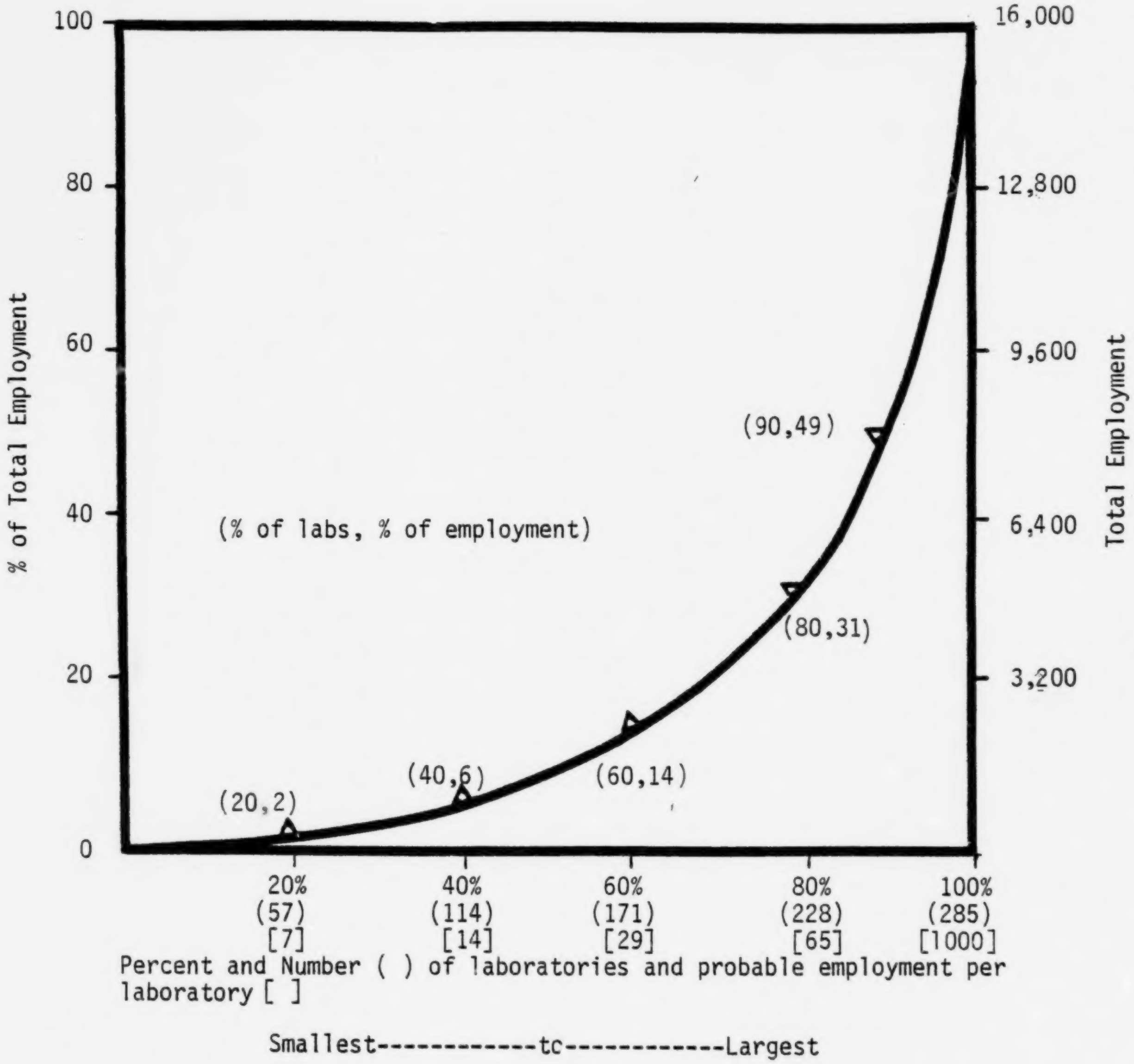
1/ Other laboratory types which contribute to testing supply, but which do so less significantly than do contract or captive laboratories are discussed in Section 9--, Other Laboratories.



Source: Francke, 1981.

Exhibit III-1. Distribution of employment (Lorenz curve) for toxicology testing laboratories, 1981.

Research Institute (SRI International); certain university laboratories would also be included here. Industry sources usually refer to the following five firms (presented in alphabetical order) as those among the leaders of the for-profit laboratories:

- Bio/dynamics, Inc.
- Hazleton Laboratories of America, Inc.
- International Research and Development Corporation (IRDC)
- Litton Bionetics, Inc.
- Raltech Scientific Services

Captive laboratories, divisions or subsidiaries of firms, perform in-house testing for their companies. Importantly, however, some also perform contract testing, a practice which reduces the importance that ownership characteristics may play in determining a laboratories' testing capabilities. The survey data indicate that captive laboratories perform a sizeable amount of contract work.

Nonetheless, about 34 percent (about 100 laboratories) of all toxicology laboratories are classified as independent, contract firms. The remaining 180 to 190 laboratories are owned and controlled by parent firms and perform work both in-house and on a contract basis.

7. Type of Business

The aggregate industry work, categorized as in-house or contract testing, is divided into about 58 percent contract and 42 percent in-house. An individual laboratory's work mix will, however, vary extensively from this industry mean:

Type of Business	% of Laboratories
In-house (100% in-house)	24
Primarily in-house (71-99% in-house)	12
Combined (30-70% in-house)	11
Primarily contract (71-99% contract)	19
Contract (100% contract)	34
	100

While no data exist from which to estimate overall industry trends, industry literature suggests an increasing contract business. This primarily reflects:

- the lack of in-house facilities,
- the strain placed on existing in-house capacity by long-term studies, and
- the belief of some companies that regulators favor data from unbiased outsiders who have no self-interest in the chemical being tested.

Industry sources suggest, as well, that much expansion has taken place in captive laboratories. Several reasons are given among which are (1) better quality control, (2) improved scheduling, and (3) cost savings.

8. Important Qualitative Factors

Two qualitative factors are important to an understanding of the chemical testing industry: the quality of testing and the potential breakthroughs in testing methods.

Toxicological testing is a service industry and, as is true of other service industries, its quality considerations play an extremely important role. Indeed, these quality considerations are consequential, non-price determinants when a prospective customer chooses a particular laboratory. This importance is emphasized, also, by various measures that have been taken since the industry has shown evidence of uneven testing quality. In answer to this, for instance, EPA has proposed Good Laboratory Practices and Testing Guidelines. Other recent quality control efforts have also been instituted: The Toxicology Laboratory Accreditation Board has been established to accredit laboratories; the American Board of Toxicology now certifies toxicologists; and the Food and Drug Administration promulgates and enforces the Good Laboratory Practices standards. The apparent dilution of testing resources has raised the potential for a decline in the industry's quality of testing.

The second important qualitative factor is that the industry's potential for significant breakthroughs in testing methods could markedly alter the mix of its critical resources. The reality of today's testing methods for chronic effects, for instance, is that such tests take three or more years to complete, cost hundreds of thousands of dollars, and can still be inconclusive in terms of estimating human risk, particularly at low-exposure levels.

A need clearly exists for quicker, less expensive, and more reliable testing methods for both oncogenic and non-oncogenic effects. Much research has been conducted in this area, particularly using in-vitro methods to screen for mutagenic and carcinogenic effects. (Bates, 1977; Dagani, 1980; Freed, 1979; U.S.H.E.W., 1979.) While some of this research has been promising and some disappointing, a significant breakthrough would change testing methods and would have the potential to consequentially redefine the market for toxicological testing and change the required mix of underlying resources.

9. Other Laboratories

The foregoing analysis concentrated on laboratories which are capable of providing commercial toxicology testing services. These included independent contract laboratories (profit and non-profit), captive laboratories, and selected university laboratories. Three additional classifications of chemical testing laboratories are part of the supply of the industry's chemical testing service: other university, government, and foreign laboratories. These sources, which were not included in the survey or in the foregoing analysis of supply, are briefly discussed below.

University laboratories are evidently becoming increasingly interested in providing contract testing services. Because some are included on toxicology testing lists and are seeking commercial testing work, a selected number of university laboratories were included in this study of the toxicology testing industry. Others also operate toxicology laboratories; they, however, are used for basic research and teaching and would not be available to perform testing in response to government regulations. These laboratories may, however, still play an important role in determining the supply of chemical testing services, for they too compete with contract and captive laboratories for critical resources.

Government facilities can be considered as part of the chemical testing supply since considerable toxicological testing is conducted by the federal government itself; however, these facilities are restricted to addressing only governmental toxicological testing demands. For this reason, then, government toxicological testing facilities were not assessed as part of the chemical industry's testing supply. One significance of the government sector is its competition for testing resources - particularly toxicologists and pathologists.

Foreign laboratories operate on both contract and captive bases in many European countries, Japan, and Canada and compete, to some extent, with U.S. contract laboratories. (Hazleton 10K report, (SEC, 1980a.) In addition to their foreign based laboratories, multinational chemical and pharmaceutical companies do use U.S. laboratories and, hence, utilize a part of the chemical testing supply available to U.S. firms. The capacity and utilization of such multinational firms are less well documented than are U.S. facilities; thus, these laboratories were considered beyond the scope and resources of this study.

B. Testing Capabilities

1. General Areas of Testing

Toxicology testing laboratories perform health and environmental testing in four general areas that are potentially required under TSCA regulations (44 FR 16240-16292). These are:

- Mammalian (Animal) Testing
- *In-Vitro* Testing
- Environmental Effects Testing
- Chemical Fate Testing

Most laboratories are also capable of performing general product and analytical testing which may or may not be related to health and environmental testing.

The laboratory resource survey which was formative in presenting the industry profile of the preceding section also provided information on the extent of testing in the above four major test areas. As shown in

Exhibit III-2, 63 percent of the toxicology laboratories are currently performing mammalian testing. Mammalian testing accounts for 38 percent of the testing revenues generated by toxicology laboratories which is equivalent to total annual revenues of $250 million. While about one-half of the laboratories perform in-vitro, environmental effects and chemical fate testing, each area represents but a small portion of all industry testing volume: mammalian testing represents an average of 38 percent of the volume; the other three toxicology testing areas represent only 7 to 13 percent of the industry's testing.

Most of the laboratories, 81 percent, also perform standard analytical and product testing; however, such testing is much less resource intensive and, thus, generates a smaller share of testing revenues than mammalian testing, 30 percent versus 28 percent. Thus, while about 28 percent more laboratories provide analytical and product testing than mammalian testing (a component of biological testing), the former generates 20 percent less testing revenues than mammalian testing. Product and analytical testing may also serve as a management tool, for those areas can be more easily expanded or reduced depending upon the level of utilization in the health and environmental testing areas.

Within the four major health and environmental testing areas, many specific types of tests exist and provide a further understanding of the capabilities of the testing industry. These are discussed in detail in the following sections according to their general test areas.

2. Mammalian Testing

Mammalian testing is that component of biological testing which utilizes the highest order vertebrates in its testing procedures. [For this study, it is equivalent to "animal testing" for it does include a limited use of poultry (non-mammalians)]. Mammalian testing capabilities can be categorized by (1) the types of tests it performs and (2) the types of mammals (animals) it utilizes. While these categories are not entirely separate, they are convenient and logical measures with which to address industry capability and resource issues.

a. Types of tests

The general category of mammalian (animal) testing includes seven testing types:

(1) acute
(2) subchronic
(3) chronic
(4) reproductive
(5) teratogenic
(6) oncogenic
(7) histopathological

Exhibit III-2. Estimated number of U.S. toxicology laboratories and their volume of testing (dollars) by testing area, 1981

Testing area	Toxicology laboratories		Volume of testing			
			Total testing		Toxicological testing 1/	
	(%)	(No.)	(%)	($ mil.)	(%)	($mil.)
Mammalian	63	180	38	250	56	250
In-vitro	51	150	12	80	18	80
Environmental effects	51	150	13	80	18	80
Chemical fate	48	140	7	40	9	40
Product and analytical (toxic and non-toxic testing)	81	230	30	200	NA	NA
TOTAL			100	650	100	450

1/ Excludes product and analytical testing which may or may not be related to toxicological testing.

NA = Not Applicable

Source: Francke, 1981.

In addition, within the acute, subchronic, and chronic types listed above, several major sub-types of tests can also be identified:

Acute

- acute oral toxicity
- acute dermal toxicity
- acute inhalation toxicity
- primary eye irritation
- primary dermal irritation
- dermal sensitization
- acute delayed neurotoxicity

Subchronic

- oral dosing
- 90-day dermal toxicity
- inhalation toxicity
- neurotoxicity

Chronic

- oral
- dermal
- inhalation
- parenteral

To completely assess the ability of the commercial testing industry to perform its present and potentially required testing, the capability of the laboratories that conduct these specific sub-types of mammalian testing must be known. For example, almost 94 percent (about 170) of laboratories performing mammalian testing offer acute oral toxicity testing. In contrast, only 55 percent (or 100) of the mammalian testing laboratories conduct the more resource-consuming acute inhalation toxicity tests and a comparatively low 51 percent perform delayed neurotoxicity tests. In the remaining areas of acute testing, over 80 percent of the mammalian testing laboratories (over half of all toxicology laboratories) perform the tests. Exhibit III-3 summarizes the specific mammalian testing capability of the surveyed laboratories.

Further review of Exhibit III-3 indicates that fewer laboratories perform inhalation toxicity and neurotoxicity tests, be they acute, subchronic or chronic than perform the other sub-types of tests. This is attributable to the extensive capital required to secure the needed specialized equipment and laboratory space and to the relatively limited numbers of personnel available to perform the more sophisticated protocols required in these areas. There may also be relatively less demand for inhalation and neurologic tests as they may be delayed until the less complex oral and dermal tests have been performed.

This analysis is limited as only the number of laboratories performing the specific tests is known. Not known is the capacity for each specific type of test for laboratories and the industry and no direct data are available to estimate current or future demand for these types of tests. The implications are, however, that a simple count may underestimate capacity in some areas as cross-tabulations show that about 75 percent of the firms employing over 100 persons provide acute and subchronic inhalation testing

Exhibit III-3. Percent and number of laboratories performing specific types of mammalian tests, 1981

Category or subcategory of mammalian testing	Percent of mammalian testing laboratories performing test	Percent of toxicology laboratories performing tests	Estimated number of toxicology laboratories
MAMMALIAN TESTING	100	63	180
1. ACUTE			
Oral Toxicity	94	60	170
Dermal Toxicity	87	55	160
Inhalation Toxicity	55	35	100
Primary Eye Irritation	82	52	150
Primary Dermal Irritation	87	55	160
Dermal Sensitization	83	52	150
Delayed Neurotoxicity	51	32	90
2. SUB CHRONIC			
Oral Dosing	83	52	150
90-day Dermal Toxicity	74	47	130
Inhalation Toxicity	42	27	80
Neurotoxicity	46	29	80
3. CHRONIC			
Oral	74	47	130
Dermal	66	42	120
Inhalation	36	23	60
Parenteral	64	40	110
4. REPRODUCTION	63	40	110
5. TERATOGENIC	64	40	110
6. ONCOGENIC	63	40	110
7. HISTOPATHOLOGIC	70	44	130

Source: Francke, 1981.

where as only 15 to 30 percent of firms employing 10 persons or less provide these tests. Thus, although no estimate can be derived, actual testing resources or supply could be relatively abundant . Furthermore, if demand for inhalation or neurotoxicity tests is relatively low, then such test capabilities may be adequate.

b. Animals used

Small rodents are the most commonly used animals for toxicity testing. An estimated 97 percent of the laboratories performing mammalian tests use such small rodents as mice, rats, hamsters and gerbils, and an average laboratory requires an on-going inventory of about 11,000 rodents. Rabbits, the next most frequently used animals, are utilized by 95 percent of the mammalian testing laboratories, and facilities' average inventory is about 230. The incidence of the use of these and the other animals and average number in use and inventory per laboratory are shown below.

Test Animal	Percent of mammalian laboratories using animal	Average number of animals in use and inventory
Small rodents (mice, rats, hamsters, gerbils)	97	11,000
Rabbits	95	232
Guinea Pigs (large rodents)	91	180
Dogs	63	186
Cats	50	28
Primates	37	257
Poultry	43	148
Large Domestic Animals (e.g. cows)	29	52

These data provide an estimate of the animal resources normally in use in mammalian testing laboratories. For example, these data indicate that the industry will normally maintain about 1.9 million rodents either in tests or inventory at any given time. The normal maintenance levels for other animals would be 40,000 for rabbits, 29,000 for guinea pigs, 31,000 for dogs, 3,000 for cats, 17,000 for primates, 11,000 for poultry and 3,000 for large domestic animals.

3. In-Vitro Testing

In-vitro testing is that form of biological testing in which the test is conducted outside of an organism (as opposed to in-vivo, or "within-the-organism" testing). The major types of specific in-vitro tests are:

- tests for detecting gene mutations (e.g. Ames test, mouse-lymphoma assay)
- tests for detecting chromosomal aberrations (e.g. cytogenetics, dominant lethal assay)

- tests for detecting primary DNA damage (e.g. DNA repair, unscheduled DNA synthesis)
- tests of physiological parameters (e.g. biochemical, cytology)

A summary of the frequency of specific in-vitro testing in the toxicology testing industry is shown in Exhibit III-4. The number of laboratories performing each specific test is between 75 and 105 laboratories out of a total of 150 in-vitro laboratories and 285 commercial toxicology laboratories.

4. Environmental Effects Testing

Environmental effects testing is conducted to determine the toxic effects of chemicals on entire aquatic or terrestrial ecological communities. It differs from mammalian and in-vitro testing which are conducted specifically to assess the toxicity of chemicals to humans. About 150 toxicology laboratories perform environmental effects tests. The two major categories of environmental effects tests performed by toxicology laboratories are: (1) terrestrial testing and (2) aquatic testing. Of the laboratories offering environmental effects testing, 27 percent (40 laboratories) perform only terrestrial testing, 33 percent (50 laboratories) perform aquatic testing and 40 percent (60 laboratories) perform both. (Francke, 1981.)

5. Chemical Fate Testing

Chemical fate testing determines the chemical persistence of a compound and indicates that chemical's ability to retain its physical, chemical, and functional characteristics in the environment through which it is transported and distributed (44 FR 16240-16292). Chemical fate testing is provided by an estimated 140 laboratories and involves two major types of studies:

- laboratory studies (e.g. hydrolysis, photo-degeneration, soil metabolism)
- field studies (e.g. field dissipation, bioaccumulation)

These two types of tests are carried out by the industry in the following proportions. Laboratory studies only are conducted by 36 percent (50 laboratories) of the chemical fate testing laboratories; 13 percent (20 laboratories) perform only field studies and 51 percent (70 laboratories) of the chemical fate laboratories perform both. (Francke, 1981.)

C. Capacity and Utilization

The foregoing review of the general nature and testing capabilities of the toxicology industry (Sections A and B) has provided necessary, but insufficient information for determining the ability of the industry to

Exhibit III-4. Laboratories capable of performing specific *in-vitro* tests, 1981.

In-vitro tests	Percent of laboratories providing *in-vitro* testing	Percent of all toxicology laboratories	Estimated number of laboratories
	%	%	No.
Detecting Gene Mutation	67	35	100
Detecting Chromosomal Abberations	52	27	80
Detecting Primary DNA Damage	50	26	75
Physiological Parameters	71	37	105
ALL TYPES	100	51	150

Source: Francke, 1981.

perform additional testing in response to TSCA or other government regulations. The determination requires an evaluation of the industry's capacity and its level of utilization.

1. Laboratories with Excess Capacity by Type of Test

The toxicology testing industry currently exhibits excess capacity in all areas of general testing. 1/ Surveyed laboratories indicated that 73 percent of the mammalian testing laboratories have additional capacity. In addition, 78 percent of the *in-vitro* laboratories; 84 percent of the environmental effects laboratories, and 75 percent of the chemical fate laboratories have excess testing capacity. These survey responses are consistent with industry literature which indicates recent rapid industry expansion and probable excess capacities (Veraska, 1980.)

2. Amount of Excess Capacity

Surveyed laboratory representatives who indicated excess capacity were also asked to specify the extent of that excess. Specifically, for each general testing area, they were asked if they had 1-10 percent, 10-20 percent, 20-30 percent, or over 30 percent excess capacity. Of those with excess capacity, 41 to 54 percent indicated 30 percent or more excess capacity, depending upon the testing area considered.

Exhibit III-5 summarizes the industry's overall excess capacity levels by test area. Depending upon the test areas considered, laboratories can perform between 18 and 22 percent more testing. Given these levels, industry utilization would appear to be about 80 to 85 percent. Many laboratories operate at less than 75 percent utilization.

Analysis was also done to determine if the level of excess capacity varied according to size of laboratories. Crosstabulation and chi-square tests indicate that an insignificant relationship exists between the employment size of laboratories and their level of excess capacity. Large firms, then, are just as likely to have excess capacity as are small firms.

Unfortunately (for regulatory planners), the current disequilibrium between test demand and capacity cannot be expected to exist indefinitely, and only extensive analysis can determine the industry's critical future capacity levels. (This issue receives more detailed attention in Chapter V: "Conceptual Supply-Demand Model Development.")

1/ "Excess capacity" as used here refers to the industry's ability to perform additional work. No "unit" of excess capacity is established. "Utilization" is simply the ratio of current operating level (indexed at 100) to the sum of operating level plus excess capacity. If excess capacity is 20 percent, then utilization would be 100/(100+20) or 83 percent.

Exhibit III-5. Summary of excess testing capacity for general areas of testing

GENERAL AREAS OF TESTING Excess Capacity	Laboratories		Excess capacity in area (%)
	%	No.	
MAMMALIAN TESTING			
No excess capacity	27	50	0
1 - 10% (5%) 1/	12	20	1
10 - 20% (15%) 1/	15	30	2
20 - 30% (25%) 1/	15	30	4
Over 30% (35%) 1/	31	50	11
Total	100	180 2/	18
IN-VITRO TESTING			
No excess capacity	23	30	0
1 - 10%	12	20	1
10 - 20%	13	20	2
20 - 30%	11	20	3
Over 30%	41	60	14
Total	100	150 2/	20
ENVIRONMENTAL EFFECTS TESTING			
No excess capacity	16	20	0
1 - 10%	10	15	1
10 - 20%	20	30	3
20 - 30%	9	15	2
Over 30%	45	70	16
Total	100	150 2/	22
CHEMICAL FATE TESTING			
No excess capacity	25	35	0
1 - 10%	13	20	1
10 - 20%	18	25	3
20 - 30%	11	15	3
Over 30%	33	45	12
Total	100	140 2/	19

1/ Assumed group mean used for all general areas of testing.

2/ Estimated total number of laboratories in industry by category, 1981.

Source: Francke, 1981.

D. Resource Supplies and Constraints

The potential supply of toxicology testing for regulatory actions is a function of the availability of the industry's critical resources: its professionals, animals, equipment, supplies, laboratory space, and capital.

1. Resource Supplies

a. Professionals

The underlying professional manpower resources, including pathologists, toxicologists, and veterinarians, are critical determinants of the industry's capacity to conduct toxicology testing. This study section briefly describes the characteristics and availability of industry professionals.

(1) Pathologists. Pathologists--both general and veterinary pathologists--are primarily responsible for the examination of animal tissue as a means of determining the toxicological effects of the chemical substances that are under study.

A number of pathologists are board-certified members of the American College of Veterinary Pathologists whose training and education, prior to eligibility for certification, spans eleven to thirteen years and includes college, veterinary school, and five years of professional experience. Exhibit III-6 indicates the employment placement of the 486 board-certified veterinary pathologists who were registered members of the ACVP in 1980. (ACVP, 1981.) One hundred ten (23 percent) of the members were employed by industry (their specific employing organizations were not identified by the ACVP registry data) and, according to toxicological industry personnel, an unspecified, increasing number of the categorized university and government veterinary personnel are also employed by the industry laboratories on a part-time basis. Industry personnel indicate, also, that toxicological laboratories also employ other veterinary pathologists who are fully professional, or "board eligible" for certification but not "board-certified."

Clearly, the toxicological industry's supply of pathologists is not limited to veterinary pathologists alone. Indeed, other pathologists now examine animal tissues within the industry. In its January, 1978, report, the American College of Veterinary Pathology estimated that in addition to a probable 100-200 non-registered veterinary pathologists (many with Ph.D.'s) working in drug and toxicity testing programs, approximately 500-600 non-registered non-veterinary pathologists were also so employed. Doubtless, then, the industry does and can continue to address its need for veterinary pathology services by seeking supporting personnel. Although some industry personnel view with mixed attitudes the use of "other" pathologists, such professionals do work in the industry. Too, technicians can be used for such tasks as slide screening to supplement the work of the veterinary pathologists (although, this too receives mixed reviews).

Exhibit III-6. Distribution of board-certified veterinary pathologists by employment sector

Sector	Number	Percent
UNIVERSITY		
Teaching	91	19
Research	79	16
Other	19	4
Total	189	39
INDUSTRY		
Research	91	19
Other	19	4
Total	110	23
GOVERNMENT		
Federal	23	5
State, local, international	32	7
Total	55	12
FOREIGN (outside U.S.)	40	8
PRIVATE PRACTICE	29	6
RETIRED	17	3
OTHER	9	2
UNKNOWN 1/	37	7
Grand Total	486	100

1/ Membership list data insufficient to identify employer.

Source: 1980 American Veterinary Medical Association Directory.

(2) Toxicologists. As Exhibit III-7 shows, the Society of Toxicology (SOT) membership registry indicates a possible total of 1,103 toxicologists in 1980. Universities employed the greatest number of SOT members--313 or 28 percent, closely followed by private industry which employed 300 SOT members or 27 percent. The remaining members were employed by government (14 percent), firms outside the U.S. (10 percent), commercial testing laboratories (7 percent), and other institutions, including hospitals, trade associations, and private foundations (3 percent). Five percent of the members were retired. (Employment type could not be identified for six percent of the society members.) A workshop held in April, 1978, sponsored by NIEHS, the Chemical Industry Institute of Toxicology (CIIT), EPA, and the Conservation Foundation, reported that SOT membership represented about 20 percent of professionals working in the field of toxicology and estimated the supply of toxicologists at about 5,000 professionals. The workshop further estimated that an additional 1,000 professional toxicologists were needed to meet immediate demand. (Gusman, 1978.)

The Society of Toxicology initiated the formation of the American Board of Toxicology, Inc. -- a certifying board for general toxicologists. As of August, 1980, 373 persons had sat for the qualifying examination and 216 had passed. In addition, certifying boards for toxicologists exist in highly specialized areas such as veterinary toxicology, medical toxicology, and clinical toxicology. NIEHS is currently developing a taxonomy to classify toxicologists and their training programs and to project the supply to toxicologists into the coming year.

The degree of lateral mobility in toxicology and related disciplines is generally high. One report estimates that "additional toxicologists can be trained from other biological sciences in 2-3 years." (Weig, 1980.)

(3) Veterinarians. The proposed TSCA testing guidelines require that test animals' care and welfare be the responsibility of a veterinarian who is certified or eligible for certification by the American College of Laboratory Animal Medicine (ACLAM) and who has at least two years of experience. (The experience requirements for ACLAM eligibility include four years beyond the veterinary degree.) There are between 280 and 290 members of ACLAM, but the number of other eligible veterinarians is unknown. Whether or not a shortage of animal care veterinarians occurs as TSCA is implemented will depend on the additional number of available ACLAM-eligible (but not certified) veterinarians, and, more generally, on the overall supply of veterinarians.

In 1979, there were over 33,000 veterinarians in the U.S. (including those inactive or retired) of which 30,706 were members of the American Veterinary Medical Association. (Anon., 1980e.) As shown in Exhibit III-8, almost 80 percent of the association membership was in private practice in 1979, and only 12 percent was listed under the category of "other, including veterinary services."

Exhibit III-7. Distribution of Society of Toxicology members among employment sectors

Sector	Number	Percent
Universities	313	28
Private Industry	300	27
Government (all levels)	155	14
Foreign (outside U.S.)	105	10
Commercial Testing Laboratories	75	7
Retired	58	5
Other Institutions 1/	34	3
Unknown 2/	63	6
Total	1,103	100

1/ Includes hospitals, private foundations, and trade associations.

2/ Membership list data insufficient to identify employer.

Source: Society of Toxicology - Membership List 1980.

Exhibit III-8. Type of employment of members of the American Veterinary Medical Association

Type of employment	Estimated number	Percent
Private Practice	26,100	79
Large animals	2,300	7
Small animals	12,200	37
Mixed	11,600	35
Other Practice		
Regulatory veterinary medicine	1,000	3
Veterinary public health	300	1
Military veterinary services	300	1
Other, including laboratory services	4,000	12
Retired, not in practice, or status not reported	1,300	4
Total	33,000	100

Source: Unpublished data from American Veterinary Medical Association, Schaumburg, IL, 1980.

In the past two decades, the annual number of veterinary school graduates has more than doubled, from 824 in 1961 to 1,712 in 1979. (Anon., 1980 e); however, the evidence of a shortage of veterinarians does exist. In a recent survey of academic veterinary science departments, 35 percent reported a perceived critical veterinarian supply shortage (NRC, 1978.)

b. Capital

Capital availability is of obvious significance. It will frequently determine the adequacy of other critical resources; it is critical, also, for expanding laboratory testing capabilities and maintaining an organization's operations during periods of reduced demand or unusually sharp competition. Unlike that for professionals and other testing resources (i.e., animals and laboratory equipment), the capital resource availability for the toxicological industry is dependant upon competition with other industries as each makes demands upon the nation's general capital resources. This condition, too, determines the industry's capital resource availability. It should be noted, however, that capital is always available; its relative availability is reflected in capital's price--interest rates.

c. Other resources

Other resources that may affect the capacity for toxicological testing include space, animals, and equipment.

(1) Availability of space. Because many toxicological studies required their own animal rooms, laboratory space was a potentially constraining resource when testing demand increased during the mid- and late-1970's. For this reason, and because chemical companies have been increasing their in-house capacity and new firms have entered the industry, much expansion in laboratory facilities occurred in recent years. This has reduced the concern about the availability of this resource for the near future. (See Section A-3.)

(2) Availability of laboratory animals. According to the Animal Resources Division and Veterinary Resources Branch of NIH, no serious problem exists for the availability of conventional laboratory animals other than primates. A senior staff veterinarian for the Division of Veterinary Services, Department of Agriculture, agreed that the supply and demand balance for test animals is fairly equal; he did caution, however, that specific animals are, at times, in short supply.

A shortage can occur for a variety of reasons. At times, a laboratory's otherwise stable and adequate test animal inventory can be decimated or made unacceptable for testing by the outbreak of a disease or the failure of laboratory security. Sudden testing trends can call for an unusually high and an immediately unanswerable demand for particular animals or species. State and local legislation can result and, in some areas has resulted, in laboratories being restricted in their procurement of "random source" animals (i.e., cats and dogs received from pounds) for testing purposes. And, too, the availability of non-human primates can be constricted and, at times, become a problem of long-term shortage by the passage of statutes in the U.S. and in their country of origin that place these animals in "threatened" or "endangered" species categories.

The apparent supply and demand balance for test animals, despite the large increases in testing in recent years, is due to the large number of commercial breeders of laboratory animals and to the practice of research organizations breeding their own animals. An official at the Department of Agriculture reports that between 180 to 200 companies are licensed under the Animal Welfare Act of 1966 to sell animals for research purposes. In addition, this figure does not include those facilities breeding only rats and mice (currently not required to register with the Department of Agriculture). Preliminary assessment by the Department, however, indicates that approximately fifty breeders of rats and mice also supply laboratory needs.

(3) Availability of equipment. The equipment needed for toxicological testing has become increasingly specialized, with computer-based information systems now being used in both the in-life and pathology phases of testing. Although testing laboratories are now confronted with a wide array of equipment of varying levels of sophistication, no evidence has uncovered suggesting that equipment availability is a constraint to growth. Equipment decisions are normally made through standard capital budgeting processes.

2. Resource Constraints

a. Critical Expansion Factors

During the survey conducted for the present study, laboratory officials were asked to rate the importance of various resources in constraining expansion of toxicology testing in the U.S. Specifically, they were asked to rate factors on a scale from one to seven (one is "not critical" and seven is "very critical"). Out of the six major resource areas listed above and in Exhibit III-9, the availability of capital was rated the most critical constraint to expansion with an average rating of 5.0 and, furthermore, 31 percent rated it "very critical." Availability of laboratory space and professionals were a distant second at 3.9 and 3.8, respectively, and only 11 to 12 percent of the respondents listed these as "very critical" for expansion. Animals, equipment, and supplies were generally not considered to be critical constraints.

Further analysis was done to determine which types of professionals--toxicologists, veterinary pathologists, and pathologists--were the more critical manpower constraint. In cases where professionals were a critical constraint (rated 4 or over), toxicologists were rated as the most critical constraint, followed by veterinary pathologists, and then pathologists. The average rating for each class of professional was as follows.

Exhibit III-9. Summary of the critical nature of the availability of resources to industry expansion

Availability of:	Critical nature of availability							Average value
	Not critical	------------	------------Critical	------------	------------	Very critical		
	1	2	3	4	5	6	7	
	------------	------------	------------	(percent)	------------	------------	------------	
Professionals	17	14	15	13	19	11	11	3.8
Animals	46	23	16	6	4	1	3	2.1
Equipment	40	22	18	7	4	3	4	2.4
Supplies	47	23	12	7	5	3	3	2.2
Laboratory Space	18	9	17	13	17	13	12	3.9
Capital	9	5	8	12	17	18	31	5.0

Source: Francke, 1981.

Toxicologists.........5.34 (1 = not critical, 7 = very critical)
Vet. Pathologist......5.06
Pathologists..........4.23

An analysis of variance statistical test indicated these means were significantly different at the 95 percent confidence level.

Note again that these specific manpower constraints were rated only when the overall manpower constraint was rated 4 or higher; thus, the above means would be biased upward if compared to the other resource constraints, and they are, therefore, not comparable.

Finally, the survey results may understate the critical nature of professional manpower resources. A combination of three conditions suggest this. First, the timing of the survey may have caused capital availability to be overrated as interest rates are at a near term high, and a survey taken during lower interest rates could show relatively higher concern for manpower resources. Second, current demand for testing and manpower resources appears to be significantly below the supply of testing capabilities and the current concern for manpower resources to expand testing is relatively low. Third, the responses reflect individuals' judgements relative to their own individual firms and not the industry as a whole; an individual firm through salary and work incentives can attract new professionals from another firm much faster than the industry can attract new professional entrants. Industry analysts have also suggested that manpower could be a serious constraint in upcoming years as significant lead time is required for training. In summary, this implies professional manpower resources may deserve close monitoring and additional study.

b. Most Constraining Resources

To further clarify questions of constraint to industry supply expansion, laboratory representatives were asked to identify the most critical constraint to expansion. The results were consistent with the prior analysis and showed capital to be the most critical resource. The relative frequency that various resources were named as most critical is shown as follows.

Constraining Resources	Percent of representatives naming most critical
Professionals	19
Animals	1
Equipment	1
Supplies	0
Laboratory Space	10
Capital	46
Other	23
Total	100

Note that the open-ended "other" was the category with the second greatest frequency as "most critical". This "catch-all" constraint category reflected such concerns as:

- government regulations
- demand/market/competition factors
- shortage of non-professional personnel
- public antipathy toward animal testing

These are not significant resource constraints *per se*, but they indicate that, in addition to the general resource needs of the industry, market perception and business climate are strong concerns for those laboratories considering future expansion. [1]

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[1] More detailed survey data and analysis on this and other topics are available in this study's supplemental report: *Toxicology Laboratory Testing Industry--A Survey Analysis*, prepared for EPA by Daniel W. Francke, *et al*, Development Planning and Research Associates, Inc., November 1981.

IV. DEMAND FOR TOXICOLOGICAL TESTING

The demand for toxicological testing stems from several sources. Testing, for both research and commercial purposes, is conducted by governments, universities, other research institutes, and the private sector laboratories. The commercial testing which is conducted by the private sector is divided into testing that is either directly or indirectly induced by regulation, a distinction necessarily vague since it depends upon the intent, not always discernible, of those ordering the tests. For this demand study, testing is considered directly induced by regulation if it is reported to the government in connection with regulatory activities under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Toxic Substances Control Act (TSCA), or the Federal Food, Drug and Cosmetic Act (FFDCA). Examples of indirectly induced testing includes tests motivated by the Resource Conservation and Recovery Act, the Clean Water Act, and the Clean Air Act as no testing is specified by these acts. In this chapter are estimates of the annual demand for testing that can be expected over the next several years. Section A outlines a methodology for estimating demand. Sections B through D estimate the demand for toxicological testing which is directly generated by FIFRA, TSCA, and FFDCA. These sections describe the regulatory processes and their required tests, and estimate the number of chemicals passing through these regulatory processes. This information is combined to produce an estimate of the total amount of testing demand induced by statutory regulations. Section E includes a discussion of the commercial demand for testing not directly induced by regulation. Research demand for toxicological testing is discussed in Section F. Section G summarizes the chapter and aggregates, to the extent possible, the direct and indirectly induced demands.

In order to completely characterize the demand side of the toxicological testing market, both the non-testing demand for the resources used in testing as well as the testing demands themselves must be determined. Toxicological testing requires several different resources: laboratory space, animals, equipment and supplies, support personnel, technicians, and professionals. At any time, the availability of each of these resources for use in toxicological testing is limited by other, non-testing demands on those resources. Such non-testing demand is not, however, equally consequential for all resources. Some resources, such as toxicologists and certain types of equipment, are so specialized that toxicological testing constitutes virtually the entire demand for that resource. For other resources (e.g., secretaries, computer programmers) testing demand constitutes but an insignificant proportion of the total demand for such resources. A previous study of toxicological testing (ICF, 1980), on the other hand, found the availability of professional manpower--toxicologists, veterinarians, and veterinary pathologists-- to be a major constraint to growth in testing capacity. (The markets for professional manpower were analyzed in the preceding chapter on the supply of toxicological testing resources. Therefore, the demand for professional manpower is not discussed further in this chapter.)

A. Methodology of Demand Assessment

The primary requirement for a satisfactory methodology is that it include all sources of testing demand, for the exclusion of any significant source of demand could seriously bias the estimate of the balance between supply and demand. As an aid to ensuring that all sources of demand were covered, testing demand was divided into three components:

- regulatory demand,
- commercial, nonregulatory demand, and
- research demand.

The regulatory demand for toxicological tests is primarily generated by three federal laws under which chemicals are regulated: TSCA and FIFRA, both administered by the U.S. Environmental Protection Agency, and FFDCA, administered by the Food and Drug Administration. Although all commercially marketed chemicals are covered under one of these three laws, not all such testing need be reported to the applicable regulatory agencies: tests must be reported only (1) when a chemical is initially approved or (2) when testing is specifically required by the agency. Firms may do further tests for their own purposes on existing chemicals, and firms may conduct tests of new chemicals which, for one reason or another, are not introduced commercially. For instance, during their research and development stage, potential new products may be discarded for a variety of reasons including unfavorable test results. In either case, what is of importance is that the magnitude of this commercial, nonregulatory demand cannot be assessed merely by looking at these chemicals submitted for government approval. In addition to the testing demand directly induced by regulations under TSCA, FIFRA, and FFDCA, and other testing demanded by industry, toxicological testing is also done in the course of scientific research by universities, governments, and other research organizations.

The estimates of demand for toxicological testing employed in this study stem from a variety of sources. Regulatory demand was derived from records on new chemical introductions kept by the primary regulatory agencies, EPA and FDA. Commercial, nonregulatory demand was estimated from conversations with industry personnel, from research on chemical innovation research, and from public sources. Research demand was estimated from public documents and from conversations with members of research organizations.

The estimates made in this chapter are intended to project the average annual amount of toxicological testing that will be required over the next several years. An estimate based upon long-term experience is more stable than one based upon the testing demand for a single year. In spite of any estimate's accuracy, however, budget restrictions, the state of the economy, changes in the discretionary authority of the regulatory agencies, and the growth and altering circumstances of chemical firms can cause relatively large, short-term variations in testing demand.

B. Demand for Pesticide Testing under FIFRA

This section provides the estimated average annual demand for pesticide testing required by FIFRA regulations over the next several years. It does not include that which may be carried out for other purposes: pesticide manufacturers, for instance, may conduct a substantial amount of pesticide testing not connected with FIFRA requirements. The demand for testing which will not be directly induced by FIFRA is discussed in Section E.

The section describes (1) the FIFRA regulatory process, including the recently implemented data call-in program, and (2) the FIFRA requirements for the toxicological testing of pesticides under FIFRA. The section then estimates the numbers of pesticides that are expected to enter the regulatory process during the next several years. Finally, the section, by combining data on the types of tests required and the number of pesticides to be regulated, includes estimates of the demand for toxicological testing under FIFRA.

1. The Regulatory Process

Regulation of pesticides under FIFRA has been in effect since 1947, and under EPA's jurisdiction since 1970. Before being sold, each new active ingredient and formulation containing that active ingredient must be registered with EPA. During that registration process, health, safety and efficacy studies are reviewed by the Agency before registration is permitted. Currently some 38,000 pesticides are registered with EPA, of which about 1,400 are active ingredients and the remainder formulations of those ingredients. The 1972 amendments to FIFRA directed EPA to "publish guidelines specifying the kinds of information which will be required to support the registration of a pesticide" and to reregister all currently registered pesticides. (FIFRA, 1972.) To fulfill this mandate, EPA issues guidelines which present the specific tests appropriate for health and safety studies, the suggested protocols for running the tests, and the descriptions of the data needed to support registration. The toxicological testing guidelines which describe the specific tests needed for product registration and the protocols for conducting those tests were proposed in 1978 (EPA, 1978). Their final versions were to be issued in 1981.

In addition to developing such guidelines for toxicological and other types of testing, EPA is designing standards for the entire registration process. Under the registration standards system (also known as the "generic standards system"), EPA intends to develop registration standards which cover those pesticide products which contain the same active ingredient. Each standard will be of two parts: one will cover an active ingredient and its manufacturing-use products [1], and one part will cover all end-use products (formulations) which contain that active ingredient. Each part will, in turn, contain four components:

- a statement of the agency's regulatory position defining the acceptable uses of a pesticide and establishing restrictions on the composition of products,
- a statement of the rationale for that position,
- an assessment of all data reviewed by the Agency, including an assessment of the costs and benefits consequent to the use of that pesticide, and
- a listing of the tolerances for those pesticides which leave residues in food or feed (under authority of FFDCA rather than FIFRA).

Data are on agency file for those products which are currently registered. But, for two reasons, these data are not likely to be adequate for reregistration. EPA now requires more data than it did when many products were first registered, and the data that are available frequently reflect studies now regarded as fundamentally inadequate or otherwise unacceptable for product use in currently registered pesticides (Chemical Regulation Reporter (CRR) 1980a). Since many studies take several years to complete, a commensurate time may be necessary to issue complete standards for these pesticides. Rather than delaying issuance of any standard for these pesticides, EPA will issue interim standards which address those issues for which insufficient data exist, list the studies which must still be performed, and establish a timetable for their performance.

For those currently registered pesticides for which standard development has not yet begun--those based on the 598 active ingredients on the registration standards list--EPA has implemented a data call-in program. The goals of this program are to identify the data that will be needed for the preparation of a registration standard and to ensure that pesticide manufacturers begin the required testing. The data call-in program concentrates on studies that take more than six months to complete: oncogenicity, teratogenicity, reproduction, and chronic effects. Further testing requirements, primarily short-term ones, will be determined for each pesticide at the time EPA begins developing an applicable registration standard.

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[1] Manufacturing-use products are products intended for end use as pesticides only after reformulation or packaging.

Under the data call-in program, EPA will evaluate the data already on file with the Agency to determine if they are sufficient to support registration. When they are not, EPA will provide each registrant of the pesticide with a notification which includes:

- the long-term toxicology data requirements for that chemical,
- that portion of the data requirements which is not currently available, and
- the rejection criteria which define minimally acceptable protocol and methodology requirements for existing studies.

After receiving the notice, the registrant will have ninety days to demonstrate that either appropriate steps are being taken to secure the required data (including replacing those data which do not meet the rejection criteria) or that procedures have been implemented for reaching agreement with other registrants concerning joint data development. The registrant will have to satisfy the requirements either by submitting new or citing existing data and certifying the acceptability of that data when judged against the rejection criteria or by agreeing to conduct new studies. Unless such procedures are instituted, EPA can suspend the product's registration. The agency's call-in process includes EPA's review of all proposed test protocols and schedules that are submitted by the registrant. Following the agency's and registrant's agreement on schedules and protocols, the call-in process will be completed. After the completion of the call-in process, the agency will continue to monitor the progress of the studies until they are completed. Registrants are given four years from the date of the notice to provide all necessary data. (CRR 1980b and 1981a.)

2. Requirements for Toxicological Testing

EPA published an Economic Impact Analysis of its testing guidelines in September, 1978 (EPA, 1978b.) which contained the Agency's estimates of the costs of the proposed testing requirements and the estimated numbers of tests that would have to be performed for new and currently registered pesticides. This section reviews that analysis and updates the estimates in the light of recent events and data. Exhibit IV-1 shows these revised estimates.

The specific requirements for the testing of each new or currently registered pesticide are based on that product's intended use and its probable environmental exposure. For example, pesticides that remain as residues in food or that otherwise involve repeated human exposure require tests that evaluate its hazard to humans and animals. However, this is the theoretical basis for EPA's testing guidelines and the Agency's estimates of testing demand could not be based solely on such a basis. Instead, EPA extrapolated historical data to estimate the number of pesticides that would require various kinds of tests. (EPA, 1978b.) For example, when extrapolated, the application volumes from 1971-1978 suggested that

Exhibit IV-1. EPA estimates of the proportion of pesticide active ingredients and formulations requiring a given toxicological test

Test name	EPA's estimate of percent of new products requiring test 1/		Estimated percent of registered products with acceptable data of this type on file with EPA 2/	
	Active ingredients	Formulated products	Active ingredients	Formulated products
	Percent			
1. Acute Oral Toxicity	98	99	1-10	1-10
2. Acute Dermal Toxicity	98	99	1-10	1-10
3. Acute Inhalation Toxicity	15	75	0	0
4. Primary Eye Irritation	99	99	75	75
5. Primary Dermal Irritation	99	99	75	75
6. Dermal Sensitization	100	50	0	0
7. Acute Delayed Neurotoxicity	7	N/A	80	N/A
8. Subchronic Oral Dosing	24	N/A	99	N/A
9. 21-Day Dermal Toxicity 3/	21	N/A	10	N/A
10. 90-Day Dermal Toxicity 3/	1	N/A	0	N/A
11. Subchronic Inhalation Toxicity	11	N/A	0	N/A
12. Subchronic Neurotoxicity	1	N/A	0	N/A
13. Chronic Feeding	24	N/A	50	N/A
14. Oncogenicity	31	N/A	approx. 50% in rat studies 5% in mouse studies	N/A
15. Teratogenicity	33	N/A	50	N/A
16. Reproduction	33	N/A	50	N/A
17. Mutagenicity	33	N/A	0	N/A
18. Metabolism--Single Dose	34	N/A	45	N/A
19. Metabolism--Multiple Dose	24	N/A	35	N/A

1/ EPA, "Proposed Guidelines, Economic Impact Analysis," 43, Federal Register, Sepbember 6, 1978, Tables 2.3, 5, 6, 8, 10, 11, 13, and 14, and p. 39647.

2/ Estimated by EPA staff, registration division, in early 1980; communicated to ICF by Gary Ballard, OPP. Estimates for chronic feeding, oncogenicity, and reproduction updated after conversations with Gary Ballard and William Burnham in January 1981.

3/ Under the Guidelines, these two tests may be required of formulations on a case-by-case basis, but EPA did not estimate the proportion of formulations which would require these tests.

NA = Data not available.

approximately fifteen new applications for the registration of active ingredients would be received (or approved) in a given year in the 1980's. (EPA, 1978b.) Furthermore, each of these fifteen new active ingredients would require product chemistry testing, and a smaller proportion individual tests for environmental, fish and wildlife, and human and domestic animal hazard evaluations. The estimated proportions of individual tests needed were based on the experience of use patterns, chemical classes, and exposure routes of currently registered products.

For currently registered products, EPA assumed that approximately 5-10 percent of the necessary data would be available in its files. (Ballard, 1980.) (For human and domestic animal hazard testing, EPA estimated separate proportions for each individual test.) Finally, for many formulations, both new and currently registered, the Agency believed testing requirements would be less extensive and made separate estimates.

EPA's estimates assumed that new active ingredients and their formulations would follow the same use and exposure patterns as do the currently registered pesticides; therefore, the Agency imposed new product data requirements that reflected past registration data needs. (EPA, 1978b.) The Agency's assumption, however, may not be valid, because of the changing economics of the pesticide industry and the increasing costs for testing. For example, as testing requirements become more stringent, and, hence, more costly, pesticides for use on minor crops may become economically infeasible. Thus, EPA's assumptions about the use distribution of future pesticides may not be accurate. At the moment, however, the point is essentially one of caution, for no definitive data exist which would authoritatively amend EPA's estimates. The present study continues to employ EPA's assumptions.

Current information suggests, too, that EPA's estimates of the tests to be performed on currently registered pesticide may be incorrect. EPA originally assumed that relatively high percentages of currently registered products would have acceptable data on file from long-term studies--chronic feeding, oncogenicity, teratogenicity, and reproduction. However, the Agency's Scientific Advisory Panel has argued that under EPA's rejection criteria, nearly all older chronic effects studies would have to be redone. (CRR, 1980c.) Although Agency pesticide program officials suggest that the Scientific Advisory Panel's concern may be overstated, the rejection criteria are still being modified, and even when in final form, will still be subject to interpretation by EPA. Because of this uncertainty and because the data call-in program is just beginning, it is too early to tell how the criteria will be applied. It does appear, however, that previous estimates of the suitability of existing data from chronic studies were optimistic. (Ballard, Burnham, 1980.)

3. Number of Pesticides to be Regulated

Exhibit IV-2 shows the estimated number of newly registered and reregistered products to be tested in the early 1980's. As noted below, these estimates are highly uncertain.

Exhibit IV-2. Estimates of the annual number of pesticides undergoing tests

I. New Products	
a. active ingredients	15 1/
b. formulated products	3,000 2/
II. Currently Registered Products	
a. active ingredients	50
b. formulated products	1,750

1/ The average annual number of new active ingredients applying for registration, FY 1971-FY 1980.

2/ The average annual number of new formulations applying for registration FY 1971-FY 1980.

Source: Registration Division, Office of Pesticide Programs, EPA.

In its economic impact analysis, EPA estimated that fifteen new, active ingredients and 3,000 new formulations would be introduced each year in the early 1980's--the average annual numbers of new active ingredients and formulations for which registration was sought during the period FY 1971-FY 1978. Data from FY 1979 and FY 1980 do not change this estimate. 1/

The situation for the reregistration of currently registered pesticides is somewhat more complex. EPA originally hoped that 50 standards and 100 early notifications of future standard development could be issued each year (EPA, 1978b). Assuming the tests begin upon receipt of early notification, then about 75 active ingredients would be undergoing tests annually. The experience of the early 1980's registration standards program, however, suggests that EPA's estimate of 100 early notifications and 50 standards per year was optimistic. In February 1980, the Agency estimated that in 1980, 10-20 standards would be issued and in 1981, 20-40 standards. (CRR, 1980d.) EPA actually managed to complete but six standards in FY 1980 and by the end of June, 1981, added four and was close to completing six additional standards. (CRR, 1980b, 1981b.) Starting in 1983, the Agency hopes to complete 35 standards a year. (CRR, 1980k.)

Although the delay of standard-setting decreases the number of pesticides per year for which tests are done, the data call-in program works to increase that number. EPA hopes to complete the call-in program (i.e., the establishment of testing schedules) by early 1982 (CRR, 1980b.); however, the Agency does believe that four years or 1984 is a more realistic estimate of the time required for completion. (Werdig, 1981.) A four-year schedule for completing the data call-in program would result in about 135 completions per year. Because registrants are given four years from the date of the notice to provide the missing data, a four-year schedule for completing the data call-in program could result in that testing taking an eight-year period for completion. Assuming that all testing associated with the 55 active ingredients not covered by the call-in program (those for which registration standard development has already begun) is also completed over this eight-year period, the reregistration process will generate testing on about 75 active ingredients per year in the 1980's.

However, testing may not proceed this quickly. Registrants can request delays in testing schedules for legitimate reasons, including the lack of testing capacity. (Werdig, 1981.) The Agency is well aware that TSCA testing may strain testing capacity, and is prepared to be flexible in approving necessary testing schedule delays. (CRR, 1980b). Although that flexibility is beneficial to producers and consumers of pesticides, it does complicate efforts to estimate the volume of testing demand. The data

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1/ In FY 1979, registration was sought for 17 active ingredients and 378 formulated products. In FY 1980, the figures were 9 and 1,671. The low number of formulated products for which registration was sought is regarded as an aberration by EPA, one caused by changes in internal procedures. It is expected that registration will be sought for over 5,000 formulated products in FY 1981. (Ballard, 1980.)

call-in program and the actual standard-setting process are assumed to generate testing on about 50 chemicals per year during the early 1980's. That estimate is highly uncertain.

The present study assumed a mean of 49 formulations for each currently registered active ingredient to calculate the annual testing demand for the pesticide products. Although EPA provided no estimate of formulations in its economic impact statement, the ten registration standards issued thus far have an average of 49 formulations. 1/

Finally, in its 1978 Economic Impact Analysis, EPA assumed that products representing 10 percent of the total sales volume of active ingredients would not be economically viable under the guidelines for registering products and would be withdrawn by their manufacturers. (EPA, 1978b.) Because high volume products are the more likely to be reregistered, the assumption argues that fewer than 90 percent of the products would be reregistered. In fact, for the first ten standards, registrants responded to protect their registrations for about 72 percent of the 159 product registrations affected. (CRR 1981c.) This study, therefore, assumed that, on the average, tests will be conducted on 35 formulated products (72 percent of 49) for each active ingredient.

4. Demand for Toxicological Testing

In summary, then, Exhibit IV-3 combines all the information in Exhibits IV-1 and IV-2 to predict the number of each type of toxicological test that would be conducted per year in the early 1980's under the assumptions given above. For example, Exhibit IV-1 shows that 33 percent of active ingredients require teratogenicity tests annually; thus, about 5 teratogenicity tests will be conducted on new active ingredients. The table also indicates that about 33 percent of the 50 currently registered pesticides also require teratogenicity tests; however, since about 50 percent of these products are assumed to have acceptable data already on file with EPA, only 16 percent of the 50 currently registered pesticides would require new teratogenicity tests. Because none of the active ingredients for which registration standards have been developed have been totally withdrawn by their manufacturers, it is assumed that no active ingredients will be withdrawn. However, as stated above, only about 72 percent of the formulated products covered by the first ten registration standards were protected by their registrants.

1/ Of the ten products for which registration standards have been issued, one (deet) has 239 products, another (dichlone) has 68, and the rest have between 17 and 35. As would be expected, the sample variance is quite high. Therefore, the use of the estimates mean number of formulated products--49--is logical but conjectured.

Exhibit IV-3. Pesticide-related testing demand: Estimated annual number of human and domestic animal hazard tests

	Number of tests by application type				
	New		Currently registered		
Test name	active ingredients	Formulated products	Active ingredidents	Formulated products	Totals
1. Acute Oral Toxicity	15	2,970	44	1,123	4,152
2. Acute Dermal Toxicity	15	2,970	44	1,123	4,152
3. Acute Inhalation Toxicity	2	2,250	8	945	3,205
4. Primary Eye Irritation	15	2,970	13	312	3,310
5. Primary Dermal Irritation	15	2,970	13	312	3,310
6. Dermal Sensitization	15	1,500	50	630	2,175
7. Acute Delayed Neurotoxicity	1	0	1	0	2
8. Subchronic Oral Dosing	4	0	0	0	4
9. 21-Day Dermal Toxicity	3	2/	9	1/	12 1/
10. 90-Day Dermal Toxicity	0	2/	1	1/	1 1/
11. Subchronic Inhalation Toxicity	2	0	6	0	8
12. Subchronic Neurotoxicity	0	0	1	0	1
13. Chronic Feeding	4	0	6	0	10
14. Oncogenicity	5	0	12	0	17
15. Teratogenicity	5	0	8	0	13
16. Reproduction	5	0	8	0	13
17. Mutagenicity	5	0	16	0	21
18. Metabolism--Single Dose	5	0	9	0	14
19. Metabolism--Multiple Dose	4	0	8	0	12

1/ Under the Guidelines, these two tests may be required of formulations on a case-by-case basis, but EPA did not estimate the proportion of formulations which may require these tests.

2/ Under the Guidelines, these two tests may be required of formulations on a case-by-case basis, but EPA did not estimate the proportion of formulations which would require these tests.

Entries in this table were arithmetically derived from Exhibits IV-1 and IV-2 and are rounded to the nearest unit.

Finally (and as a further example of the present study's estimate rationale) of the 1,750 formulated products covered by the regulation standard and data call-in program each year, 99 percent (1,732) would require primary eye irritation tests. Of these, 25 percent (433) would not have acceptable data on file with EPA, and, of these, 72 percent (312) would be defended by their manufacturers. Therefore, based on these assumptions, 312 primary eye irritation tests would be required for formulated products covered by registration standards and the data call-in program in the early 1980s. Where Exhibit IV-1 gives a range of figures, the higher number was chosen.

C. Demand for Toxicological Testing Under TSCA

Under TSCA, EPA is given the authority to regulate all chemical substances and mixtures not regulated under FFDCA, FIFRA, or the Atomic Energy Act. Toxicological testing may result from regulations promulgated under two different sections of TSCA. Under Section 4, EPA can require the testing of any chemical substance or mixture for which there are insufficient data to determine whether the chemical substance or mixture presents an unreasonable risk of injury to health or the environment. Under Section 5, any firm seeking to manufacture a new chemical substance or to use an existing chemical substance in a significantly different way must submit a notice of its intentions to EPA. If EPA finds a reasonable basis to conclude that production or use of the chemical will present an unreasonable risk of injury to health or the environment or that the data are insufficient to determine whether such an unreasonable risk exists, the Agency can prohibit or limit the manufacture and use of the substance. Although no testing is required *per se* under Section 5, testing may be generated if firms feel that it is useful in avoiding restrictive EPA action against production and use of the substance.

This section of the present study estimates the testing demands expected as a result of Sections 4 and 5 of TSCA. Because the regulation of chemicals under TSCA is relatively recent, few historical data on which to base projections exist. The actions that have been taken under each of the two sections are discussed below, the factors which might produce future changes in the implementation of the law are evaluated, and the resultant information is then used to estimate the testing demand incident to TSCA.

1. Section 4 Testing

Although testing can be required for any substance which meets the requirements of Section 4, under Section 4(e) the agency is required to give priority consideration to a list of chemicals developed by the Interagency Testing Committee (ITC). This list is to be updated at least every six months by the Committee, and within twelve months after a chemical is added to the list, EPA must either initiate a rulemaking to require testing or publish in the *Federal Register* its reasons for not doing so. Since its initial report in October, 1977, the ITC has presented seven additional lists to EPA, recommending a total of 46 chemicals or categories of chemicals for a variety of tests. By law, the list can contain no more than 50 chemicals or categories of chemicals at any one time.

In July, 1980, EPA proposed its first test rule covering substances on the ITC list. At that time, EPA proposed that chloromethane be tested for oncogenicity and structural teratogenicity and that a representative sample of the chlorinated benzenes be tested for oncogenicity, structural teratogenicity, reproductive effects, and subchronic effects. Although the ITC had recommended doing so, EPA did not require that chloromethane be tested for acute toxicity. The Agency deferred decisions on whether to require chloromethane to be tested for neurotoxicity, behavioral teratogenicity, and mutagenicity, and whether to require the chlorinated benzenes to be tested for neurotoxicity, behavioral teratogenicity, mutagenicity, and metabolic effects. At the same time, EPA decided not to require health effects testing for acrylamide, another substance on the ITC list. (CRR, 1980e; EPA, 1980.) These decision actions are shown in Exhibit IV-4.

In June, 1981, EPA proposed test rules for three more chemicals from the ITC list: dichloromethane, nitrobenzene, and 1,1,1-trichloroethane. EPA proposed that dichloromethane be tested for acute dermal sensitization and reproductive effects, that nitrobenzene be tested for structural teratogenicity and behavioral effects, and that 1,1,1-trichloroethane be tested for structural teratogenicity. In addition, EPA will perform the initial mutagenicity test itself, because although it believes that sequenced testing would be appropriate, no criteria for progressing from initial testing to higher level testing are available. EPA will propose higher tier tests if needed based on an analysis of lower tier results. (EPA, 1981.)

a. Requirements for toxicological testing

Information on the types of tests to be required under Section 4 is not limited to the actions already taken by TSCA. The ITC's testing recommendations provide information on the tests that EPA might require for chemicals which have not yet been acted upon by EPA. As shown in Exhibit IV-5, oncogenicity, mutagenicity, teratogenicity, and other chronic effects testing are recommended for more than two-thirds of the 46 chemical substances and categories on the eight ITC lists. If these recommendations were adopted by EPA, testing demand estimates could be drawn from the ITC lists. As shown in Exhibit IV-6, EPA accepted 10 of 28 of the ITC's recommendations. In the case of acrylamide, however, EPA concluded that a consistent neurotoxic effect is demonstrated at a sufficiently low level that further testing is not necessary. Any restrictions which would significantly limit neurotoxic effects would, therefore, also provide significant protection from other health effects. In addition, Dow has assured EPA that it plans to conduct oncogenicity tests. (CRR, 1980f.)

Exhibit IV-4. Section 4 test rules, acrylamide, chloromethanes, chlorinated benzenes, nitrobenzenes and 1,1,1-trichloroethane

	Onco-genicity	Muta-genicity	Structural Teratogenicity	Reproductive effects	Subchronic/ chronic toxicity	Acute toxicity	Neuro-toxicity	Behavioral teratogenicity	Metabo-lism
Acrylamide	-	-	-	-	-	-	-	-	-
Chloromethane	x	D	x	-	-	-	D	D	-
Dichloromethane	-	x 1/	-	x	-	x	-	-	-
Mono- and Dichlorinated Benzenes:									
Monochlorobenzene	-	D	x	x	x	-	D	D	D
o-Dichlorobenzene	-	D	x	x	x	-	D	D	D
p-Dichlorobenzene	-	D	x	x	x	-	D	D	D
Nitrobenzene	-	x 1/	x	x	-	-	-	-	-
Tri-, Tetra-, and Penta-Chlorinated Benzenes:									
1,2,4-trichlorobenzene	x	D	x	-	x	-	D	D	D
1,2,4,5 tetrachlorobenzene	x	D	x	x	x	-	D	D	D
Pentachlorobenzene	x	D	-	x	x	-	D	D	D
1,1,1-trichloroethane	-	x 1/	x	-	-	-	-	-	-
Total	4	3	8	7	6	1	0	0	0

1/ To be performed by EPA.

D = Decision to propose testing deferred
x = Testing proposed.

Source: EPA, "Chloromethane and Chlorinated Benzenes Proposed Test Rule; Amendment to Proposed Health Effects Standards," 45 Federal Register, p. 48524, July 18, 1980; Chemical Regulation Reporter, July 11, 1980, p. 355.

Exhibit IV-5. ITC testing recommendations

Test	Number of items for which test is recommended	Percentage of total number of items on ITC list 1/
Oncogenicity	35	76
Mutagenicity	34	74
Teratogenicity	36	78
Other Chronic Effects 2/	32	70
Reproduction 2/	6	13
Developmental Effects	1	2

1/ An item can be a chemical or a category of chemicals. There are 46 items on the first seven ITC lists.

2/ Reproduction is often included explicitly among other chronic effects by the ITC, and it may be included implicitly in other cases. In only four cases is it mentioned separately.

Source: Reports of the Interagency Testing Committee.

Exhibit IV-6. Comparison of ITC testing recommendations and EPA test rules

Chemical substance or category	Onco-genicity	Muta-genicity	Terato-genicity	Chronic effects
Acrylamide				
ITC Recommendation	x	x	x	N
EPA Test Rule	N 1/	N	N	N
Chloromethane				
ITC Recommendation	x	x	x	x
EPA Test Rule	x	D	x	N
Dichloromethane				
ITC Recommendation	x	x	x	x
EPA Test Rule	N 2/	N 3/	N	N 3/
Mono- and Di-chlorinated Benzenes				
ITC Recommendation	x	x	x	x
EPA Test Rule	N	D	x	x
Nitrobenzene				
ITC Recommendation	x	x	N	N
EPA Test Rule	N 2/	N 3/	x	N 3/
Tri, Tetra-, and Penta-chlorinated Benzenes				
ITC Recommendation	x	x	x	x
EPA Test Rule	x	D	x	x
1,1,1-Trichlorethane				
ITC Recommendation	x	x	x	x
EPA Test Rule	N 2/	N 3/	x	N 3/

1/ One of the reasons that EPA cited for not requiring testing for acrylamide was that Dow plans to conduct oncogenicity testing of the chemical.

2/ EPA will do the initial mutagenicity testing itself, but may propose other tests later.

3/ EPA stated that the oncogenicity testing of these substances being performed by the National Cancer Institute should be sufficient for EPA's needs for these tests. Therefore, no additional testing was proposed.

D = Decision to propose testing deferred.
x = Testing proposed.
N = Testing not proposed.

Source: Exhibit IV-4 and reports of the Interagency Testing Committee.

For dichloromethane, nitrobenzene, and 1,1,1-trichloroethane, EPA is not proposing further testing because the National Cancer Institute is conducting tests sufficient for EPA's purposes. EPA will conduct the initial mutagenicity tests itself (EPA, 1981).

b. Number of chemicals to be regulated

The estimate of the number of chemicals expected to undergo Section 4 testing is even more uncertain than the estimate of the types of tests that are expected under Section 4. In May 1979, EPA was sued by the Natural Resources Defense Council (NRDC) for failing either to develop test rules or to decide not to require testing for chemicals on the ITC list. In December 1980, EPA proposed a testing schedule found acceptable by the NRDC. Under this schedule, EPA must develop test rules or decide not to require additional testing for chemicals on ITC's first six lists within the next three years. Under this schedule, EPA would issue test rules for eight chemical substances from the ITC lists during the rest of 1981, and thirteen each during 1982 and 1983. (CRR, 1981d; 1980g.) Assuming that EPA does, indeed, meet the court-imposed schedule, and assuming that EPA takes action on all chemicals added to the list during the three years of the statutory deadline, the Agency would have to take action on about twenty-two to twenty-four chemicals or groups of chemicals per year (if, of course, ITC continues its past schedule). In an affidavit filed during the course of the NRDC suit, EPA estimated that it can develop test rules for fifteen to twenty chemicals per year. (CRR, 1980h.) Therefore, unless EPA devotes more resources to the development of test rules than is planned, or unless the ITC adds fewer chemicals to the list over the next few years than it previously has added, three years from now the Agency will still be behind schedule in promulgating testing requirements.

Any attempt to estimate the number of chemicals to be tested under Section 4 is further complicated by the fact that the individual items on the ITC list are both individual chemicals and categories of chemicals. Of the 46 items on the seven ITC lists, 27 consist of a single chemical substance and the other 29 items contain as many as 100 chemicals. 1/ This means that it cannot be assumed that taking action on 20 ITC items a year would result in a maximum of 20 of each type of test. This can be seen by examining Exhibit IV-4: only five ITC categories are included for structural teratogenicity tests, but eight chemicals will eventually require the tests.

However, one cannot assume that if a test is required for that category, it will be required for all chemicals (or even all commercially important chemicals) in that category. This can be seen by examining the chlorinated

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1/ Some of the categories are "open" -- they contain a potentially immense number of chemicals. For these categories, the approximate number of chemicals currently in use, or with relatively important uses, was estimated.

benzenes, for which test rules have already been proposed. Chlorinated benzenes make up two items on the ITC list, and together they consist of eleven distinct chemical substances. But testing is required for only six of those eleven (and, further, not all the tests are required for each of the six). In general, EPA does not believe that each member of a structurally related category need be tested. Instead, a representative sample can be selected that will enable EPA to evaluate the entire category. (EPA, 1980.)

c. Demand for toxicological testing

To estimate the number of tests to be generated by Section 4 test rules, this study assumed that EPA will take action on 20 items from the ITC list each year. It further assumed that the following four tests will be required of about two-thirds of those 20 items: oncogenicity, mutagenicity, teratogenicity, and chronic effects. This assumption is a product of the observation that the ITC recommended these tests somewhat more than two-thirds of the time, and in the test rules issued thus far, EPA has recommended testing to a somewhat lesser degree than the ITC had recommended. (See Exhibit IV-6.)

In addition, this study assumed that testing for reproductive effects will be required in about half of the cases. Even though reproduction tests are specifically mentioned as a separate category for only 6 of the 46 items, reproduction is specifically mentioned as a chronic effect that should be examined in 6 other cases, and it is probably incorporated implicitly under chronic effects in many other cases. It is worth noting that EPA requires testing for reproductive effects among both categories of chlorinated benzenes on the list, even though such tests were not mentioned specifically by the ITC.

On the basis of the above assumptions, this study estimated the number of chemicals to be tested from among those 20 items. The relative composition of those 20 items is assumed to be the same as the relative composition of the 46 items named on the list thus far, that is, their number of single chemicals, number of chemical categories, and number of chemicals in the chemical categories will be similar. The number of chemicals in each category on the list was obtained for all "closed" categories. (An estimate of the number of chemicals currently in commercial production, or with relatively important uses, was used for all "open" categories.) As stated above, EPA does not intend to require tests on all chemicals in a category--tests on a "representative sample" will be sufficient. About half the chemicals were tested among the chlorinated benzenes, the only two categories for which test rules have been issued thus far. It is assumed that this policy will be continued for all categories which have a relatively small number of members, i.e., a dozen or fewer--the two chlorinated benzenes categories had four and seven members--and that for the larger categories, testing will affect about one-fourth of their chemicals. Under these assumptions, EPA should require testing on about 89 chemicals per year under Section 4. The estimated number of tests is shown in Exhibit IV-7.

Exhibit IV-7. Estimated toxicological tests per year required under Section 4 of TSCA

Test	Number
Oncogenicity	60
Mutagenicity	60
Teratogenicity	60
Chronic Effects	60
Reproduction	45

Source: Exhibits IV-4, IV-5 and IV-6.

Exhibit IV-8. Toxicological testing on chemicals submitted to EPA under Section 5 of TSCA, 1980

Test	Number
Acute oral toxicity	123
Primary Dermal Irritation	110
Primary Eye Irritation	109
Dermal Sensitization	28
Ames	52
Acute Dermal Toxocity	57
Acute Inhalation Toxicity	18
Other	38

Source: ICF analysis of Section 5 notices submitted to EPA, 1981.

2. Section 5 Testing

Under Section 5 of TSCA, no EPA tests are required for approval of a new chemical. If, however, insufficient information exists to permit a reasoned evaluation of the health and environmental effects of a chemical substance, EPA may restrict the production and use of that chemical. Manufacturers, consequently, in the course of their developing and submitting new chemicals for approval, may perform toxicological tests in order to avoid restrictive actions. A survey of the public file of 383 Section 5 notices received by EPA during calendar year 1980 revealed that 535 tests were performed on the chemicals submitted (Exhibit IV-8).

Since the number of new chemicals actually submitted to EPA is roughly the number expected by the Agency, a way to estimate future Section 5 testing could be to simply accept EPA projections. However, before making such an assumption, two issues should be considered:

- Are the chemicals introduced in 1980 representative of those expected to be introduced in the future? In early 1980, Section 5 notices were filed more slowly than they were in the latter part of 1980, and the increase in submissions continued during the first half of 1981. In the first half of 1980, 153 Section 5 notices were filed, and in the second half, 230 were filed. Two explanations are reasonable. Manufacturers may have delayed submitting notices until they had a clearer idea of how the program would work. Or manufacturers may have inventoried substances still undergoing development in order to avoid the premanufacturing review process. (CRR, 1980i.) If the latter were true, then more new chemicals can be expected in future years as this effect is reduced. The number of chemicals introduced also depends on the standards set by EPA for the approval of Section 5 notices. The higher the standards, the less likely that firms will submit new chemicals for approval.

  The types of chemicals introduced in 1980 may be different than will be the types of chemicals introduced in future years. TSCA intends to direct chemical innovation away from the more to the less environmentally hazardous chemicals. To the extent that this goals is eventually realized and it results in less needed testing, the amount of testing should decline. However, this effect may be counterbalanced by other factors, as discussed below.

- Are the types of tests conducted on new chemicals introduced this year representative of the types of tests that will be conducted in years to come? As stated above, a move toward safer chemicals would probably result in fewer new tests and higher standards of approval would probably reduce the total number of chemicals introduced. However, such higher standards of approval would also increase the amount of testing done on new chemicals because

> firms producing them would seek to do a better job of convincing EPA of their chemicals safety. Thus it is not clear, *a priori*, whether the number of tests will increase or decrease. At present, guidelines exist to indicate what tests will be done on new chemicals. Under the Carter Administration, EPA did publish testing guidelines calling for the tests in the OECD premarket data set (Exhibit IV-9) to be performed on new chemicals submitted to EPA under Section 5. But more recently, the Reagan Administration blocked a decision by the OECD to make the use of that data set binding upon all member countries. (CRR, 1981e, 1981f, 1981g.)

Because the premanufacture notification program is still evolving, estimates of future testing must be uncertain. Program operations thus far suggest that the amount of future testing will be similar to that of 1980; however, 660 Section 5 notices received in the first half of 1981, rather than the 383 submitted during 1980, have resulted in demand for 922 tests arising from Section 5 notices over a recent 18 month period which is equivalent to a rate of 615 tests per year (Exhibit IV-10). It is worth noting that an error in estimating Section 5 testing demand will be less serious than an error in estimating testing demand from other sources. Section 5 tests are almost always acute tests, and those utilize fewer testing resources than do those done under Section 4 and FIFRA.

D. Demand for Toxicological Testing Under FFDCA

The Food and Drug Administration requires toxicological testing under several different regulatory programs. The Bureau of Drugs must approve all human drugs before they can be marketed; the Bureau of Veterinary Medicine must approve all new animal drugs; and the Bureau of Foods becomes involved if a drug is to be used on animals sold for consumption. All food additives and problem cosmetics are regulated by the Bureau of Foods. In this section, the demand for toxicological testing from human and animal drugs, and food additives and cosmetics is estimated.

1. Human Drugs

The government has exercised some authority over human drugs since the Pure Food and Drug Act of 1908 prohibited the sale of misbranded and adulterated foods and drugs. The Federal Food, Drug and Cosmetic Act of 1938 placed further responsibility on drug manufacturers by requiring them to prove the safety of drugs before marketing. Under its provisions, the manufacturer was required to file a New Drug Application (NDA) which included data in support of its product; however, if the FDA failed to take action within sixty days, the drug could be marketed.

The Drug Amendments of 1962 (21 U.S.C. 355) and their subsequent regulations substantially increased FDA authority over new drugs by requiring the manufacturer to file a Notice of Claimed Investigational

Exhibit IV-9. Toxicological tests in OECD minimum premarketing data set

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Acute Oral Toxicity

Acute Dermal Toxicity

Acute Inhalation Toxicity

Dermal Irritation

Dermal Sensitization

Eye Irritation

Repeated Dose Toxicity, 14-28 days

Gene Mutation

Chromosome Aberration

Source: Chemical Regulation Reporter, January 16, 1981, p. 1297.

Exhibit IV-10. Estimated toxicological testing under Section 5 of TSCA

Test	Number
Acute Oral Toxicity	212
Primary Dermal Irritation	190
Primary Eye Irritation	188
Dermal Sensitization	48
Ames	90
Acute Dermal Toxicity	98
Acute Inhalation Toxicity	31
Other	65

Exemption (IND) with the FDA before the drug could be used in human testing (21 CFR 312). In addition, new drugs had to be proved effective as well as safe. (Although drugs approved between 1930 and 1962 were not required to prove safety and efficacy under the new amendments, the FDA could withdraw approval if it received evidence to the contrary.) The obligation to prove efficacy and safety has resulted in an increase in the amount of testing.

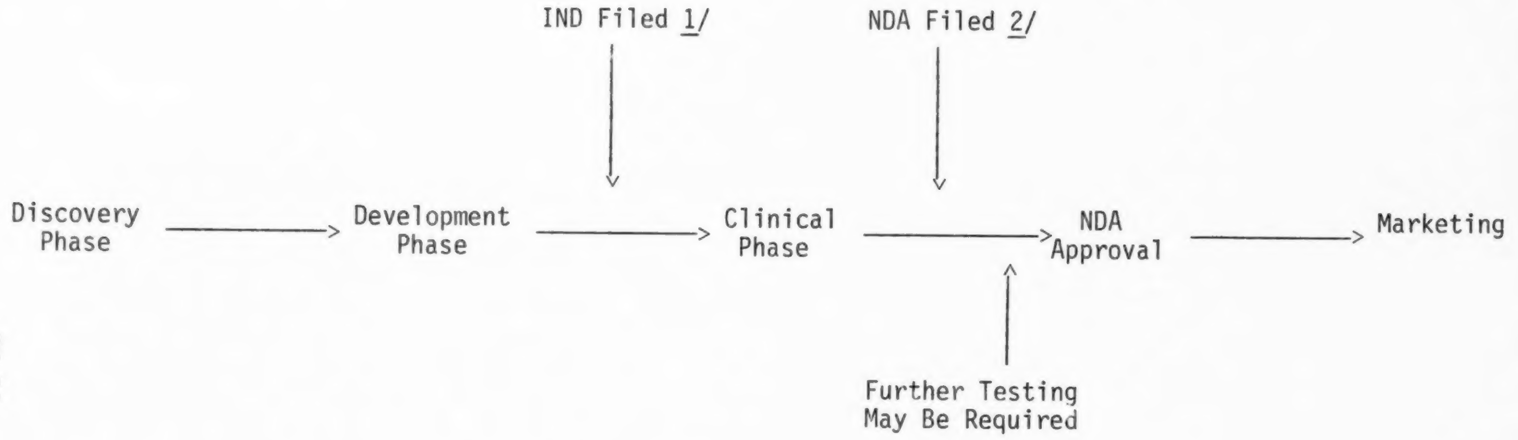
To insure quality testing, the FDA has proposed minimum standards for good laboratory practices (FDA, 1978). When an NDA is filed, the manufacturer must state that tests were carried out according to these practices or explain any differences. In addition, FDA testing guidelines are available to aid the manufacturer in designing drug development test protocols (Bureau of Drugs). Unlike the "good laboratory practices," however, these guidelines are not formal regulations and as new techniques develop, the guidelines may change.

Determining such standard procedures for drug testing is difficult for two reasons: first, much variation exists in the use and activity of the drugs. The type of testing required depends on the mode of entry of the drug, the target population, the length of treatment, and the relationship of the drug to those already in use. Second, the results of previous tests may or may not suggest what the future course of testing should be. For instance, if a drug shows ambiguous results in early tests, more testing may be required to clarify these. A drug which is pharmacologically similar to other known drugs and whose preliminary tests show no complications might progress through the testing process much faster than one which is unique. Thus, the testing program must be tailored to the individual drug. To clarify such problems, the manufacturer may contact the FDA to discuss the program as testing progresses.

Human drugs go through three phases of testing: the discovery, the development, and the clinical phases. (Hansen, 1979.) These are shown in Exhibit IV-11. The discovery phase includes the drug's basic chemical research--compound synthesis, early pharmacological studies, and research on physiopathological processes. If this early research results in a new chemical entity which shows promise, the company will move to the development phase and begin animal toxicity testing. The early research on the drug is done without formal outside review, and not until the drug is to be tested in humans, does it becomes part of the FDA public record. Thus, no formal record exists for the drugs that begin testing and are dropped before the drug enters the regulatory system. Since the testing can be quite expensive, the company must weigh the costs against the expected return at each stage in the research and development process.

In order to begin clinically testing the drug on humans, the company must file a Notice of Claimed Investigational Exemption for a New Drug (IND) (21 CFR 130). At this time, the company must file its unique in-house production information. The IND must, also, include the protocols for the planned chemical investigation. If the proper short term animal testing was performed and the results show no significant or adverse findings, the IND is granted.

Exhibit IV-11. Phases of testing of human drugs


IND Filed 1/
NDA Filed 2/
Discovery Phase
Development Phase
Clinical Phase
NDA Approval
Marketing
Further Testing May Be Required

1/ Notice of Claimed Investigational Exemption for a New Drug.

2/ New Drug Application.

Source: R. W. Hansen, "The Pharmaceutical Develoment Process: Estimates of Development Costs and Time and the Effects of Proposed Regulatory Changes," in Issues in Pharmaceutical Economics, R. I. Chien, ed. (Lexington, MA., D.C. Heath and Company, 1979.

There are three phases to clinical testing:

Phase I - drug application to healthy human volunteers, to test human toxicity and absorption
Phase II - drug application to human patients to test therapeutic value and side effects
Phase III - drug application to extensive groups of human patients to test for the drug's less common side effects.

At the same time that clinical testing is being conducted, the pharmaceutical company may also initiate long-term animal testing in preparation for marketing its product. If at the end of the clinical testing the company decides to market the drug, it must file a New Drug Application (NDA) with the FDA. The FDA reviews the results of all testing and may request additional tests. Only after the drug passes the FDA tests for efficacy and safety does FDA grant marketing approval for the drug.

a. Requirements for toxicological testing

The specific toxicological tests which each drug must undergo depend upon its intended use. In its guidelines, the FDA divides drugs into the following categories according to their method of entry to the body:

Oral or parenteral
Inhalation
Dermal
Ophthalmic
Vaginal or rectal
Combination

The type of tests for chronic toxicity required for each of these categories is listed in Exhibit IV-12. All of the drugs require acute tests in at least one species, and those drugs which will be administered orally or parenterally require acute testing in three or four species. This testing takes place before an IND is filed. Certain sub-chronic and chronic tests must be completed, also, before human testing can begin. For instance, before an oral drug can be administered to healthy humans for a period of several days up to two weeks (Phase I), it must be tested in two species for two weeks. For the drug to enter Phase II of clinical testing, it must be tested in two species for up to four weeks. Generally, drugs that are expected to be administered to the human patient for longer duration require longer periods of animal testing.

b. Number of chemicals to be regulated

The data for IND applications since the 1962 Amendments went into effect in 1963 are shown in Exhibit IV-13. No significant trend in IND applications is apparent--some variation from year to year does exist. The distribution of types of drugs on IND applications for 1979, a typical year, is shown in Exhibit IV-14. Most drugs are oral or parenteral--65 percent of the total. Drugs to be applied dermally follow with 17 percent, while drugs administered by inhalation, ophthalmic or vaginal or rectal application make up a combined total of 18 percent.

Exhibit IV-12. Summary of tests required for human drugs

			4 Subchronic and chronic tests	
1 Drug category	2 Duration of human administration	3 Acute toxicity tests (oral)	Required	To be completed before human testing phase:
Oral or Parental	Several Days	3-4 species. 1 non rodent	2 species; 2 weeks	I
	Up to 2 Weeks	"	2 species; 2 weeks	I
		"	2 species; up to 4 weeks	II
		"	2 species; up to 3 months (1 nonrodent)	III
	Up to 3 Months	"	2 species; 4 weeks	I
		"	2 species; 3 months (1 nonrodent)	III
		"	2 species; up to 6 months	NDA
	6 Months to Unlimited	"	2 species; 3 months (1 nonrodent)	I
		"	2 species; 6 months or longer (1 nonrodent)	III
		"	2 species; 12 months (nonrodent) 18 months (rodent)	NDA
Inhalation (General Anesthetics)		2 species	4 species; 5 days (3 hours/day by notice to be administered clinically	I
Dermal	Single Application	2 species, 1 non-rodent	1 species; single 24-hour exposure followed by 2-week observation	I
	Single or Short-term Application	"	1 species; 20-day repeated exposure (intact and abraded skin)	II
	Short-term Application	"	As above	NDA
	Unlimited Application	"	As above, but intact skin study extended up to 6 months	
Ophthalmic	Single Application	1 or 2 species	1 species; 3 weeks daily applications, as in clinical use	I
	Multiple Application	"	1 species; duration commensurate with period of drug administration	NDA
Vaginal or Rectal	Single Application	1 or 2 species	2 species; duration and number of applications determined by proposed use	I
	Multiple Application	"		

Source: Synopsis of "General Guidelines for Animal Toxicity Studies," FDA.

Exhibit IV-13. Annual number of IND's 1/ and NDA's 2/ filed

Year	Original IND's submitted	Original NDA's submitted	NDA's approved
1963	1,066	192	71
1964	875	160	70
1965	761	221	50
1966	715	216	50
1967	671	128	74
1968	859	108	56
1969	956	60	39
1970	1,127	87	53
1971	923	256	68
1972	902	272	42
1973	822	149	77
1974	802	129	95
1975	876	137	68
1976	885	127	101
1977	925	124	63
1978	925	121	86
1979	940	182	94
Average	884	157	68
Average 1963-1967	818	183	63
Average 1969-1973	946	165	56
Average 1975-1979	910	138	82

1/ Notice of claimed investigational exemption for a new drug.

2/ New drug application.

Source: Stanley A. Stringer, Bureau of Drugs, Food and Drug Administration.

Exhibit IV-14. Distribution of IND's by category, 1979

Category	Number	Percent of total
Oral/Parenteral	624	65
Inhalation	73	8
Dermal	161	17
Ophthalmic	86	9
Vaginal/Rectal	12	1
Combination	0	0
TOTAL	956 1/	100

1/ In 1979, 940 IND drug applications were received and some of these drugs were included in more than one testing category.

Source: Stanley A. Stringer, Bureau of Drugs, Food and Drug Administration.

If it is assumed that the future distribution of drugs among the categories will be similar to that of the past, the number of each type of test required by the IND's introduced in a particular year can be predicted. Since the IND is filed in order to begin clinical testing, then all IND drugs go through the animal testing required to reach Phase I. The tests required to reach Phase I are given in Exhibit IV-15. Ninety percent of the IND drugs never get past Phase I because (1) they produce no effective pharmacological activity in humans, (2) they have undesirable side effects, or (3) the testing program studied biological processes in humans rather than sought to develop a marketable drug. (Anon., 1978c.)

Unless the risks turn out to be greater than anticipated or commercial problems develop, NDA's will eventually be filed on the drugs entering Phase II. (Hansen, 1979.) Thus, the NDA's submitted will reflect the number of drugs that pass through human testing. In addition to the human tests, these drugs will go through the animal testing outlined in Exhibit IV-16.

c. Demand for toxicological testing

Since the number of drugs whose manufacturers have filed IND's and NDA's is known, the number of tests required for FDA approval of these types of applications can be calculated. Although data on the distribution for the NDA's are not known, the distribution should be similar to that of the IND's. Based on this distribution, Exhibit IV-17 shows the estimated number of drugs with IND's and NDA's in 1979. Combining the testing data from Exhibits IV-15 and IV-16 and the numerical data from Exhibit IV-17 results in the total number of tests shown in Exhibit IV-18.

2. Animal Drugs

The government also regulates animal drugs under the FFDCA. The approval process for animal drugs was formerly complicated by the fact that a drug could be regulated as a "new drug," an "antibiotic," or a "food additive," depending upon its intended use. Since the primary purpose of these regulations was to control products that would be used directly by humans, they did not specifically address the protection of target animals and their indirect effect on humans. The Animal Drug Amendments of 1968 drew together all of the sections of the FFDCA which concern animal drugs. In addition, the drugs which are used in food animals are subject to the regulations covering food additives.

A new animal drug is regarded as unsafe until it is approved by the FDA, and until it is approved, it is illegal for the drug to be marketed in interstate commerce. In order for the drug to be approved, the FDA must find that the drug is safe and effective for its intended use. The FDA evaluates testing results which are submitted in a New Animal Drug Application (NADA).

As with human drugs, it is difficult to describe a definitive set of testing protocols, since later phases of testing depend upon earlier results. Exhibit IV-19 outlines the general sequence of testing. The

Exhibit IV-15. Animal tests required for IND 1/ application for human drugs

Drug type	Duration of human administration	Acute tests			Subchronic tests			Vaginal/ Rectal application
		Oral	Dermal	Primary eye	Oral	Inhalation	Dermal	
		(number of tests)						
Oral/parenteral	Several days	3-4*			2*-two wks.			
	Two weeks	3-4*			2*-four wks.			
	Three months	3-4*			2*-four wks.			
	Six months	3-4*			2*-three mos.			
Inhalation	All dosages	2				4		
Dermal	Single dose	2*	1					
	Single or short term	2*	1				1	
	Short term	2*	1				1	
	Unlimited	2*	1				1	
Ophthalmic	Single	1-2		1	1			
	Multiple	1-2	1	1	1			
Vaginal/rectal	Single	1-2						2*
	Multiple	1-2						2*

* = One nonrodent test required

1/ Notice of claimed investigational exemption for a new drug.

Source: Adapted from, "Guidelines for Preliminary Toxicity Testing of Investigational Drugs for Human Use." Bureau of Drugs, Food and Drug Administration.

Exhibit IV-16. Tests required for NDA 1/ for human drugs

ORAL/PARENTERAL DRUGS

Duration of human administration	Acute oral	Subchronic oral dose 2 wks	4 wks	3 mos	6 mos	12 mos	18 mos
Several days	3-4* 2/	2					
2 weeks	3-4*		2* or	2*			
3 weeks	3-4*			2* or	2*		
6 months	3-4*					2* or	2*

INHALATION (GENERAL ANESTHETICS)

	Acute oral	Subchronic inhalation
All dosages	2	4

DERMAL

Duration of human administration	Acute oral	Acute dermal	Subchronic dermal	Dermal sensitization
Single application	2*	1		1
Single or short term	2*	1	1	1
Short term	2*	1	1	1
Unlimited	2*	1	1	1

OPHTHALMIC

Duration of human administration	Acute oral	Primary eye irritation	Subchronic application 3 weeks
Single	1-2*	1	1
Multiple	1-2*	1	1 3/

VAGINAL/RECTAL

Duration of human application	Acute oral	Vaginal or rectal
Single application	1-2	2*
Multiple application	1-2	2*

1/ New drug application. This includes the tests required for IND applications.
2/ Numbers refer to number of species in which tests are required.
3/ May be longer, depending on the expected duration of the treatment.
* = indicates that testing in one nonrodent required.
Source: Adapted from, "Guidelines for Preclinical Toxicity Testing of Investigational Drugs for Human Use." Bureau of Drugs, Food and Drug Administration.

Exhibit IV-17. Number of human drugs in each phase (1979).

Category 4/	IND applications	IND-NDA 2/	NDA 3/
Oral	624		90
Several days	(156)	133	(23)
up to 2 weeks	(156)	133	(23)
up to 3 months	(156)	134	(22)
6 months to unlimited	(156)	134	(22)
Inhalation	73	62	11
Dermal	161		23
Single application	(41)	35	(6)
Single or short-term application	(40)	34	(6)
Short-term application	(40)	34	(6)
Unlimited application	(40)	35	(5)
Ophthalmic	86		13
Single application	(43)	36	(7)
Multiple application	(43)	37	(6)
Vaginal or rectal	12		1
Single application	(6)	5	(1)
Multiple application	(6)	6	(0)

1/ Investigational new drug.

2/ New drug application.

3/ We have assumed that the distribution of NDA among the different categories is similar to the distribution of IND applications.

4/ The distribution of applications among the different categories was not available. We have assumed that the drug applications are distributed equally among the categories.

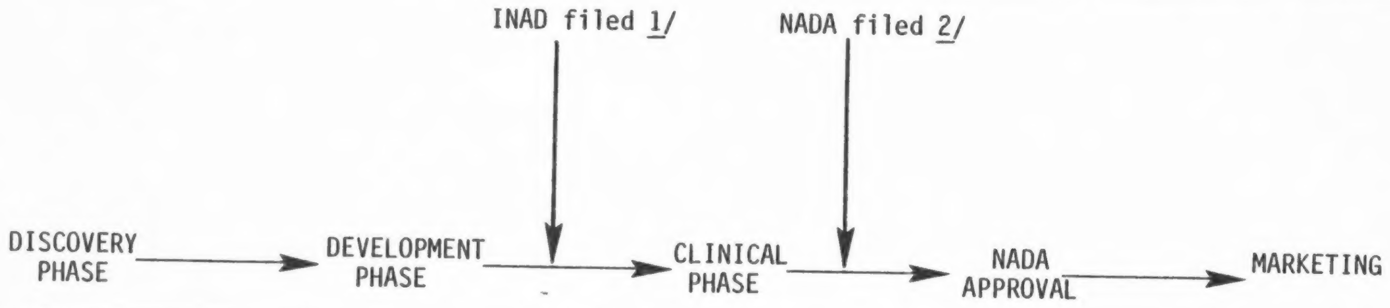
Source: Adapted from Exhibit IV-14.

Exhibit IV-18. Estimated total number of animal tests required for approval of human drugs

Acute oral toxicity			
		rodent	1,861-2,677
		nonrodent	913
Acute dermal toxicity			184
Acute inhalation toxicity			168
Primary eye irritation			86
Primary dermal irritation			137
Dermal sensitization			23
Subchronic oral			
	2 wks	rodent	202
		nonrodent	156
	4 wks	rodent	335
		nonrodent	335
	3 mos	rodent	178
		nonrodent	178
	6 mos		
	12 mos	rodent	22
		nonrodent	22
	18 mos		0
Subchronic ophthalmic application			50
Subchronic vaginal or rectal application			
		rodent	11
		nonrodent	11

Source: Exhibits IV-16 and IV-17.

Exhibit IV-19. Phases of testing of animal drugs


INAD filed 1/
NADA filed 2/
DISCOVERY PHASE
DEVELOPMENT PHASE
CLINICAL PHASE
NADA APPROVAL
MARKETING

1/ Claimed investigational exemption for a new animal drug.
2/ New animal drug application.

animal drugs go through the same first two phases of testing as do human drugs: the discovery phase--the drug's basic chemical research--and the development phase, which includes toxicological and efficacy testing on laboratory animals. If a manufacturer decides that the drug looks promising after this early animal testing, the company will apply for a Claimed Investigational Exemption for a New Animal Drug (INAD). This is necessary for two reasons: it allows the drug's distribution for clinical research, and it allows the drug to be used on food animals--meat, dairy or poultry. For instance, if a company is developing a drug to be administered in cattle feed, it must test that drug on cattle, and in order for these cattle to be slaughtered for food, the drug must be listed with the FDA as being exempt from the requirements for approval. To insure human safety, the FDA examines the resultant toxicological data and may assign a requirement for a withdrawal period--a time before slaughter during which the drug cannot be administered.

The types of tests required for a new animal drug (NAD) are listed in Exhibit IV-20, and the number of investigational new animal drugs and new animal drug applications approved in the years 1978 to 1980 are shown in Exhibit IV-21. This study could not determine how many applications were not approved. Although the testing of each drug is performed on an ad hoc basis, an upper limit for the numbers of tests can be set by assuming that each drug which has an INAD filed goes through the full range of animal toxicity tests:

(1) acute toxicity studies in mice and rats or skin and eye irritation studies,

(2) teratology studies in two rodent species,

(3) subacute or chronic study in mice, rats, and dogs,

(4) multigeneration reproduction study in rats, and

(5) sub-acute toxicity in target species.

The upper limit for the number of animal tests required for animal drugs is shown in Exhibit IV-22. No basis exists for estimating how many of the drugs require further carcinogenic studies, reproduction studies, or chronic studies. The requirements for these depend on previous test results.

3. Food Additives and Cosmetics

Though the FFDCA of 1938 prohibited the use of unsafe substances in food, it was the federal government's responsibility to prove that a substance was poisonous or otherwise deleterious. The burden of proof was shifted to the food processors with the Food Additive Amendment of 1958 which decreed that processors must demonstrate that a food additive is safe before it can be used. Under the Amendment a food additive is defined as "any substance... which may reasonably... be expected to... (become) a component

Exhibit IV-20. Tests required for animal drugs

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1. Discovery phase - Research to identify potential of chemical.
2. Dose efficacy studies

   dose-range efficacy studies
   controlled efficacy studies
   efficacy and field use experiments in three locations
3. Environmental impact analysis

   plant/fish toxicity
   stability of residues in environment
4. Acute toxicity studies in mice and rats 1/
5. Skin and eye irritation studies 1/
6. Teratology studies in two rodent species *
7. Subacute/chronic study in mice, rats and dogs *
8. Multigeneration reproduction study in rats *
9. Subacute toxicity in target species *
10. Trace drug and metabolites in different organs - target species

    radioactive study
    nonradioactive study
11. The following depend on threshold assessment:

    carcinogenic study in mice
    reproduction through weaning
        12 month necropsy
        24 month survival
        30 month survival
    6 month chronic study in dogs

1/ Assume that each drug was tested for either one or the other of these tests.

* Toxicity tests which were used in developing Exhibit IV-21.

Source: "Impact of Government Regulations on Development of Chemicals Used in Animal Production," Council for Agricultural Science and Technology Report No. 85, October 1980.

Exhibit IV-21. Annual number of INAD's 1/ and NADA's 2/ approved

Year	Original INAD's filed	Original NADA's filed
FY 1978	71	141
FY 1979	104	131
FY 1980	71	116
Yearly average	82	129

1/ Investigational new animal drug.
2/ New animal drug application.

Source: Homer R. Ransdell, Chief, Case Guidance Branch, Division of Compliance, Bureau of Veterinary Medicine, Food and Drug Administration.

Exhibit IV-22. Total number of animal tests required for approval of animal drugs 1/

Acute toxicity test 2/	
Mice	61
Rats	61
Skin or eye irritation test 2/	21
Teratology tests	164
Subacute/chronic tests	
Mice	82
Rats	82
Dogs	82
Multigenerational reproduction test in rats	82
Subacute toxicity test in target species	82
Carcinogenic study in mice	3/
Reproduction through weaning	3/
6-month chronic study in dogs	3/

1/ This is the upper limit of tests required; we assume that each animal drug for which an INAD is filed has gone through all of these tests. Based on average annual number of INADs filed, 1978-1980.

2/ We have assumed that the same percent (26%) of drugs is used for skin and eye tests in both humans and animals.

3/ No basis for estimate.

Source: Exhibits IV-20 and IV-21.

or affect the characteristics of a food. (21 CFR 570.3e.) Additives can be direct or indirect. Direct additives are added to the food to perform some function (i.e., stabilizing, preserving, improving appearance). Indirect additives are those substances which are introduced as a by-product of some process, such as their migration from packaging material. A third group of substances was exempted from the requirement of proof of safety--those generally recognized as safe (GRAS) after a long term of use. These latter additives are currently under review by the Bureau of Foods, which plans to require testing of those GRAS additives found to be suspect. The GRAS testing requirements will not go into effect until 1983. (Morgenroth, 1981.) Substances added for color purposes only were not covered until the 1958 act, and the Color Additive Amendment of 1960 requires that color additives be demonstrated safe for their intended use. Twenty-three color additives which had been provisionally approved are currently in testing. The testing had been expected to be complete by 1981, but the deadlines have been extended over the next two years. (New York Times, 11/4/80.)

As do those manufacturing human and animal drugs, the manufacturers of food additives consult with FDA toxicologists to determine testing requirements and acceptable protocols. (Kokoski, 1975.) Exhibit IV-23 shows the testing and protocol guidelines which are currently in use. Unless otherwise noted, the tests will be required for each additive and other tests are required if preliminary tests indicate a need. Teratogenicity tests, for instance, may not be required for a direct food additive unless the multigenerational reproduction study shows that the additive has affected the offspring of rats exposed to the substance. In other cases, the number of required tests increases with the expected amounts of exposure; hence, because indirect food additives with virtually no migration evidence would normally not appear in high concentration in food, they would require only acute oral testing. On the other hand, a direct food additive which could be expected to accumulate in the body in larger amounts, undergoes acute, subchronic, and multigenerational studies.

Exhibit IV-24 estimates the number of additives for which data are submitted to the FDA for approval. Combining these data with the testing required for each type of additive, yields the total number of each type of test required as is shown in Exhibit IV-25.

4. Summary: Demand for Toxicological Testing Under FFDCA

Under the FFDCA provisions, the FDA requires pre-marketing testing for human drugs, animal drugs and food additives. This study section summarizes the tests required for these three groups of drugs. The largest demand for testing is for human drugs, which must undergo both animal and extensive clinical testing before approval of the new drug application (NDA). There has been an annual average of 157 NDA's filed and 68 approved since 1962. Animal drugs also undergo both animal and clinical testing before approval, and an average of 129 new animal drug were approved each year between 1977 and 1980. Testing for food additives depends on the expected fate of the additive. Direct food additives undergo a full range of animal tests, as do indirect food additives which have extensive

Exhibit IV-23. Tests required for approval of food additives

	Direct food additive	Indirect food additive			Color additive		
		Migration 1/					
		Virtually nil	Negligible	Significant	Ingested	Topical	Sutures
Acute oral toxicity - rodent	***	X	***	***	***		
Acute oral toxicity - nonrodent	***	*	***	***			
Subchronic feeding study (90-day) - rodent			X				
Subchronic feeding study (90-day) - rat	***			***	***		
Subchronic feeding study (90-day) - nonrodent			X				
Lifetime feeding study (ca 2-year) - rodent with in-utero exposure	X			X	X		
Lifetime feeding study (ca 2-year) - rodent, for carcinogenesis	X			X	X		
Short-term feeding study (ca 6 mo. to 1 yr.) - nonrodent	X			X	X		
Multigeneration reproduction feeding study rodent	X		*	X	X		
Teratology study	*		*	*	*		
Mutagenicity screen	*		**	**	**	**	
Dermal irritation/percutaneous toxicity - rabbit						X	
Acute eye irritation (Draize test)						**	
Ocular toxicity (repeat eye instillation) - rabbit						****	
Lifetime skin painting (ca 2-years) - mouse						X	
Implantation studies -							X
a. lifetime - rate for non-absorbable sutures							
b. short-term - for absorable sutures							
c. ocular - for ophthalmic sutures							
Sensitization studies - guinea pig						X	
Sensitization studies - humans						X	
Metabolism studies	**			**	**		
Skin penetration studies						**	

1/ Food additive migration:
Virtually nil = 0.05 ppm
Negligible or insifnificant = 0.05 ppm.

X = required.
* = if indicated by available information.
** = suggested.
*** = if needed as preliminary to further study.
**** = if used in eye area.

Source: C. H. Kokoski and H. R. Gittes, "Toxicological Testing Under Varying Food and Color Additive Situations," Distributed by Bureau of Foods, FDA.

Exhibit IV-24. Annual number of additives applications for approval 1/

Type of additive	Number
Direct additives	94
Indirect additives	294
no migration (less than 0.05 ppm)	184
negligible migration (more than 0.05 ppm)	73
significant migration	37
Color additive	
ingested	10
topical	0
sutures	0

1/ 1980 data.
Source: Dr. Victor Morgenroth, Bureau of Foods, Food and Drug Administration.

Exhibit IV-25. Total numbers of tests performed for food additive approval 1/

Test	Number
Acute oral toxicity - rodent	184
Acute oral toxicity - nonrodent	2/
Subchronic feeding study (90-day) - rodent with in-utero exposure	73
Subchronic feeding study (90-day) rat	2/
Subchronic feeding study (90-day) nonrodent	73
Lifetime feeding study (*ca* 2-year) - rodent with in-utero exposure for carcinogensis and chronic toxicity	141
Lifetime feeding study (*ca* 2-year) - rodent, for carcinogenesis	141
Short-term feeding study (*ca* 6 mo. to 1 year) - nonrodent	141
Multigeneration reproduction feeding study (3 generation, 2 litters/generation, with teratology phase) - rodent	141
Teratology study	2/
Mutagenicity screen	2/
Dermal irritation/percutaneous toxicity *ca* 1 to 3 months) - rabbit	0
Acute eye irritation (Draize test)	
Ocular toxicity (repeat eye instillation) - rabbit	0
Lifetime skin painting (ca 2-years) - mouse, for carcinogenesis	0
Implantation studies - a. lifetime - rate for non-absorbable sutures b. short-term - for absorbable sutures c. ocular - for ophthalmic sutures	0
Sensitization studies - humans (repeat patch test: Draize type test) with photosensitization test	0
Metabolism studies	2/
Skin penetration studies	0

1/ Based on 1980 data. Tests which are "suggested" rather than "required" are not included.

2/ No basis for estimate.

Source: Exhibits IV-23, IV-24.

migration characteristics or color additives which are ingested. Food additives which show little migration and color additives which are used topically are screened, but they do not undergo extensive animal testing unless the results of early tests indicate a problem.

E. Commercial Demand for Testing not Directly Induced by Regulation

The demand for toxicological testing directly stemming from FIFRA, TSCA, and FFDCA requirements does not include all of the testing done for commercial purposes. In addition to the tests reported to the government under these and other laws, firms may do additional tests on existing chemicals for their own purposes (e.g., their concern over product liability). Furthermore, firms may conduct tests of new chemicals which, for one reason or another, are never introduced commercially.

Clearly trade journals and chemical industry personnel indicate that the amount of such testing appear to be substantial (CRR, 1981b, 1980.), but inadequate data are available for estimating the extent of such testing.

F. Research Demand for Toxicological Testing

Because of the multiple sources of research activity and the funding of that activity, research demand is more difficult to estimate than testing demand associated with the regulation of commercial chemical production. Toxicological research is carried out at a large number of installations. In addition, the funding for toxicological research comes from a substantial variety of research foundations and government agencies. In this section of the present study, estimates are presented for research demand only from the Department of Health and Human Services (HHS). Although toxicology-related research is sponsored by other federal agencies, the HHS funds are estimated to be at least equal to, and probably significantly greater than, the funds provided by all other federal agencies combined. (HEW, 1979.) However, analysts are unable to estimate the research demand for that toxicological testing funded by other sources.

Another difference between this study's estimates of regulatory demand and research demand is the difference in the way that the estimates are presented. In the previous three sections, of the demand estimates for each type of test were made; however, such information cannot be obtained for research demand. Instead, this study uses that which is available--the amount spent on research.

To facilitate a comparison between the results in earlier sections and those in this section, the research demand is expressed both in dollar amounts and in the numbers of oncogenicity tests that those dollar amounts would buy. The assumed relationship between those dollars and the oncogenic tests is taken from a recent survey of testing costs which found the average cost of oncogenic tests to be $655,000. (Enviro Control, 1980.) However, that figure has been increased by a 10 percent inflation margin to give a final figure of $720,000 per oncogenic test. This conversion provides a rough basis of comparison between the results here and the results in earlier sections.

The activities covered in this section include more than just basic research -- test method development and that testing conducted or paid for by government agencies are also included. The testing demand discussed in this section includes demand from EPA and FDA, agencies which were also covered in previous sections. The difference between the demands covered in this section and those covered in previous sections, however, is that in previous sections, that testing demand was generated by firms in response to regulations and in this section, only nonregulatory sources of demand are considered.

The National Toxicology Program (NTP) was formed by the Department of Health, Education and Welfare (HEW, now HHS) in 1978 to coordinate the toxicological activities of HHS agencies. Not all agencies in HHS participate in the program nor is all toxicological research in those agencies under the auspices of the National Toxicology Program. The four NTP agencies - Food and Drug Administration, National Cancer Institute, National Institute for Occupational Health and Safety, and the National Institute for Environmental Health Sciences -- originally planned to spend $219 million in FY 1980 of which $69 million was to be under the auspices of the National Toxicology Program. Other HHS agencies were to spend an additional $43 million in FY 1980. Of the total of $262 million, $114 million was to be spent on basic research, $124 million on testing, and $24 million on method development (HEW, 1979). The $262 million total is equal to the resources needed to conduct about 400 oncogenicity tests. A full range of tests are conducted by HHS agencies, but the emphasis is on oncogenicity, mutagenicity, teratogenicity, reproduction and chronic effects.

G. Summary: Demand for Resources Used in Toxicological Testing

This chapter provided estimates of the demand testing generated directly by FIFRA, TSCA and FFDCA. Commercial demand for testing not directly induced by regulation and research demand were also briefly discussed (good estimates were not obtained for either of the two latter areas). This final section, translates demand for tests into demand for the resources used in testing. The availability of the different resources used in testing may vary markedly from one resource to another; therefore, in order to completely characterize the demand side of the market, it is necessary to discuss the demand for the resources used in testing.

Exhibit IV-26 displays the resources required for several different types of toxicological tests as they are described in TSCA and FIFRA testing protocols. The estimates, developed from a separate study, are based on information obtained from testing laboratories, federal contractors, manufacturing companies that contract similar studies, personnel placement firms, industry trade associations and the contractor's own experience in the field. (Enviro Control, 1980.)

Exhibit IV-26. Resources required for toxicological testing per type of test

Personnel (Hours)	Acute oral toxicity	Acute dermal toxicity	Acute inhalation toxicity	Primary eye irritation	Primary Dermal irritation	Dermal sensitization	Acute delayed neurotoxicity	Subchronic oral dosing I	Subchronic oral dosing II	Subchronic oral dosing III	Subchronic inhalation toxicity	Subchronic neurotoxicity
Study Director	1	1	1	1	1	2	2	96	52	148	52	9
Veterinarian								16	8	24	8	
Compound Preparation Technician	1	1	8	1	1	11	1	96	52	148	90	48
Senior Technician	10	14	24	1	1	41.5	17	328.5	208.5	537	482	50
Animal Technician	10	14	24	7	4	41.5	17	328.5	208.5	537	482	50
Animal Caretaker	13	19	16	8	5	30.6	26	1032	227	1259	127	100
Clinical Lab Supervisor								46.33	33.10	79.43	16.55	
Clinical Lab Technician								138.97	99.26	238.23	49.63	
Necropsy Supervisor	7	8	7.5				13.13	54	34	88	10	18.75
Necropsy Technician	21	24	22.5				39.39	162	102	264	30	56.25
Histology Supervisor		.88	1.64				1.66	35.52	32.26	67.78	16.57	7.45
Histology Technician		3.54	6.54				6.64	148.02	111.62	259.64	66.27	29.86
Board-Certified Pathologist	7	10	12.19				16.88	163.50	114	277.50	57.50	35.63
Report Writing Supervisor								20	24	44	35	25
Report Writer	20	20	32	8	8	32	40	300	320	620	350	150
Computer Programmer								48	26	74	30	40
Computer Coder								48	26	74	30	40
Report Typists	8	10	20	4	4	16	20	200	300	500	200	50
General Secretary	1	1	1			1	1	48	26	74	26	5
Quality Assurance Inspector	1	1	8	1	1	8	8	70	52	122	80	40
Animals (Number)												
Rats	48		60						192	192	96	
Mice												
Rabbits		40		11	8							
Dogs								58		58		
Chickens							36					72
Guinea Pigs						24						

Source: Enviro Control, Incorporated, Cost Analysis Methodology and Protocol Estimates: TSCA Health Standards and FIFRA Guidelines, April 1980.

Continued . . .

Exhibit IV-26. (continued)

Personnel (Hours)	Teratogenic health effects			Reproductive effects	General metabolism	Oncogenic effects			Chronic toxicity		
	I	II	III			I	II	III	I	II	III
Study Director	24	24	48	62		208	208	416	240	208	448
Veterinarian						25	25	50	60	60	120
Compound Preparations Technician	12	16	28	60		416	416	832	480	384	864
Senior Technician	324	291	615	850	676	3142	1984	5126	3724	1011	4735
Animal Technician	324	291	615	850	386	3142	1984	5126	3724	1011	4735
Animal Caretaker	75	70.5	145.5	817.5	304	3765	1500	5265	4325	3889	8214
Clinical Lab Supervisor						8.78	8.78	17.56	52.96	39.22	92.68
Clinical Lab Technician						26.33	26.33	52.66	158.82	119.2	277.94
Necropsy Supervisor	30	27	57	33	5	100	80	180	116	54	170
Necropsy Technician	90	81	171	99	15	300	672	972	348	162	510
Histology Supervisor				76.74		183.12	168	351.12	252.88	48	300.88
Histology Technician				306.94		732.48	672	1404.48	1011.52	192	1203.52
Board-Certified Pathologist	30	27	57	109.74		625	605	1230	841	100	941
Report Writing Supervisor	10	10	20	50		50	50	100	100	50	150
Report Writing	100	80	180	400		750	750	1500	1000	750	1/50
Computer Programmer	24	24	48	120		96	96	192	160	96	256
Computer Coder	24	24	48	120		96	96	192	160	96	256
Report Typist	50	30	80	150	160	450	450	900	750	450	1200
General Secretary	12	12	24	31	20	104	104	208	120	96	216
Quality Assurance Inspector	48	48	96	80	16	224	224	448	254	230	484
Animals (Number)											
Rats	144		144	168		480		480	560		560
Mice							480	480			
Rabbits		85	85								
Dogs										58	58
Chickens											
Guinea Pigs											

Source: Enviro Control, Incorporated, Cost Analysis Methodology and Protocol Estimates: TSCA Health Standards and FIFRA Guidelines, April 1980.

Continued . . .

Exhibit IV-26 (continued)

Personnel (Hours)	Combined chronic effects I	II	III	IV
Study Director	240	208	208	656
Veterinarian	60	60	25	145
Compound Preparation Technician	480	384	416	1280
Senior Technician	3724	1011	2506	7241
Animal Technician	3724	1011	2506	7241
Animal Caretaker	4325	3889	1969	10183
Clinical Lab Supervisor	52.96	39.72	61.78	154.46
Clinical Lab Technician	158.82	119.12	185.29	463.23
Necropsy Supervisor	116	54	69.6	239.6
Necropsy Technician	348	162	208.8	718.8
Histology Supervisor	252.88	48	232	532.88
Histology Technician	1011.52	192	928	2131.52
Board-Certified Pathologist	841	100	794.6	1734.6
Report Writing Supervisor	100	50	50	200
Report Writing	1000	750	750	2500
Computer Programmer	160	96	96	352
Computer Coder	160	96	96	352
Report Typist	750	450	450	1650
General Secretary	120	96	104	320
Quality Assurance Inspector	254	230	230	714
Animals (Number)				
Rats	560			560
Mice			556	556
Rabbits				
Dogs		58		58
Chickens				
Guinea Pigs				

Source: Enviro Control, Incorporated, Cost Analysis Methodology and Protocol Estimates: TSCA Health Standards and FIFRA Guidelines, April 1980.

To illustrate how these data on resources required for toxicological testing can be used to characterize the market for individual resources, the number of Board-Certified Veterinary Pathologists required to conduct the tests directly induced by FIFRA, TSCA and FFDCA was calculated. These estimates, inherently containing a great deal of variance, are extrapolations produced by the application of assumptions to information on current testing levels, which are themselves highly uncertain. The estimates of the resources required for each test are also uncertain; the authors of a cited study suggest that a variance range of ±50 percent might be appropriate (Enviro Control, 1980). Particularly uncertain are the estimates for the resources required by FFDCA tests, for the estimates of the numbers of required tests are most uncertain for FFDCA. In addition, the protocols in Exhibit IV-26 are EPA protocols rather than FDA protocols. They may not apply to tests done under FFDCA.

The estimates of the demand for Board-Certified Veterinary Pathologists from testing directly induced by FIFRA, TSCA and FFDCA are shown in Exhibit IV-27. The total demand of 475 Board-Certified Veterinary Pathologists is only slightly less than the total number, 486, of Board-Certified Veterinary Pathologists in 1980 shown in Exhibit III-6. But the demand data do not include the demand from research,other commercial testing, teaching, and government.

Testing demands like those described in this chapter may lead to severe constraints on the availability of Board-Certified Veterinary Pathologists. However, several factors may reduce the shortage suggested by these figures. As discussed previously, there are about 700 other pathologists working in drug and toxicity testing programs. Many of these may be Board-eligible or be substitutable for Board-Certified Veterinary Pathologists. Technicians may also be substituted for some tasks.

Exhibit IV-27. Esimated demand for board-certified veterinary pathologists from FIFRA, TSCA and FFDCA

	Number of board-certified veterinary pathologists required
FIFRA	72
TSCA	
Section 4	69
Section 5	2
FFDCA	
Human drugs	117
Animal drugs	82
Food additives	133
TOTAL	475

Source: Exhibits IV-3, IV-7, IV-10, IV-18, IV-22, IV-25 and IV-26.

V. CONCEPTUAL SUPPLY-DEMAND MODEL DEVELOPMENT

The U.S. chemical testing industry provides numerous and complex toxicological testing services. From its early emphasis on foods, drugs and cosmetics chemical testing, the industry has evolved into one that tests chemical substances of all types, including pesticides, other commercial chemicals, and industrial intermediates.

Various types of laboratories comprise this industry and have contributed to its expanded capacity and testing capability--independent, captive (company), university, and government (see Chapter III). International chemical testing capabilities and laboratory capacities have grown similarly in the recent past. Collectively, these various sources or types of laboratories "supply" the toxicological testing services that are required by need and regulation.

Conversely, numerous and varied chemical developers "demand" toxicological testing services (see Chapter IV). Such testing includes both regulatory and nonregulatory demands. Government regulations, e.g., FFDCA, FIFRA, TSCA, and others, have increased the general level and complexity of toxicological testing, although many chemical companies had previously initiated comprehensive toxicological testing on a nonregulatory basis. Basic research programs often involve toxicological testing of a nonregulatory nature. Regardless of whether these sources of demand are or are not regulation-induced, they compositely reflect the aggregate demand for the chemical testing industry's services.

While the perspective is simplified, it is instructive to characterize the chemical testing industry in terms of its aggregate "supply" and "demand." Various economic relationships are theoretically assessable in aggregate terms although the magnitude and composition of the industry's testing services have and will continue to change over time. These basic supply and demand constructs will be developed initially and then integrated within a common analytical system. As explained in this chapter, the ability to represent both supply and demand in a common system is based on the delineation of underlying key resources of the toxicological testing "service" industry. Other modeling approaches are possible, although no others are developed in this study.

The principal objective of this chapter is to formulate a supply-demand model of the toxicological testing industry that can be used to measure regulation-induced economic impacts on the industry. With such a model, analysts can more readily simulate and project industry decisions and market behavior that can occur under alternative regulatory programs, such as TSCA, or under alternate economic conditions.

The preceding chapters of this study have described the baseline supply and demand conditions of the chemical testing industry, i.e., toxicology testing services, based on secondary data sources and this study's survey data. However, substantially more development is required to quantitatively define and assess the industry's traditional economic supply and demand relationships and, also, to statistically model industry behavior.

A complication of the chemical testing industry is that a broad range of toxicological tests, requiring both basic and specialized resources, may be performed by laboratories (suppliers of testing services). Hence, the "supply" of services cannot be readily quantified as a simple economic function of the "price" of tests. On the demand-side, an equally complex problem exists because the actual tests required or demanded will vary among the chemicals to be tested which, in turn, will differ through time as chemical product requirements change and chemical innovations are made.

This chapter presents a traditional economic supply-demand model of the chemical testing industry. It first presents an overall analytical system within which the industry's supply and demand constructs are defined. It then develops the supply and demand modules of that proposed analytical system. Third, it formulates a supply-demand model that has both accounting and economic subsystems. Finally, the chapter defines the model's general implementation requirements.

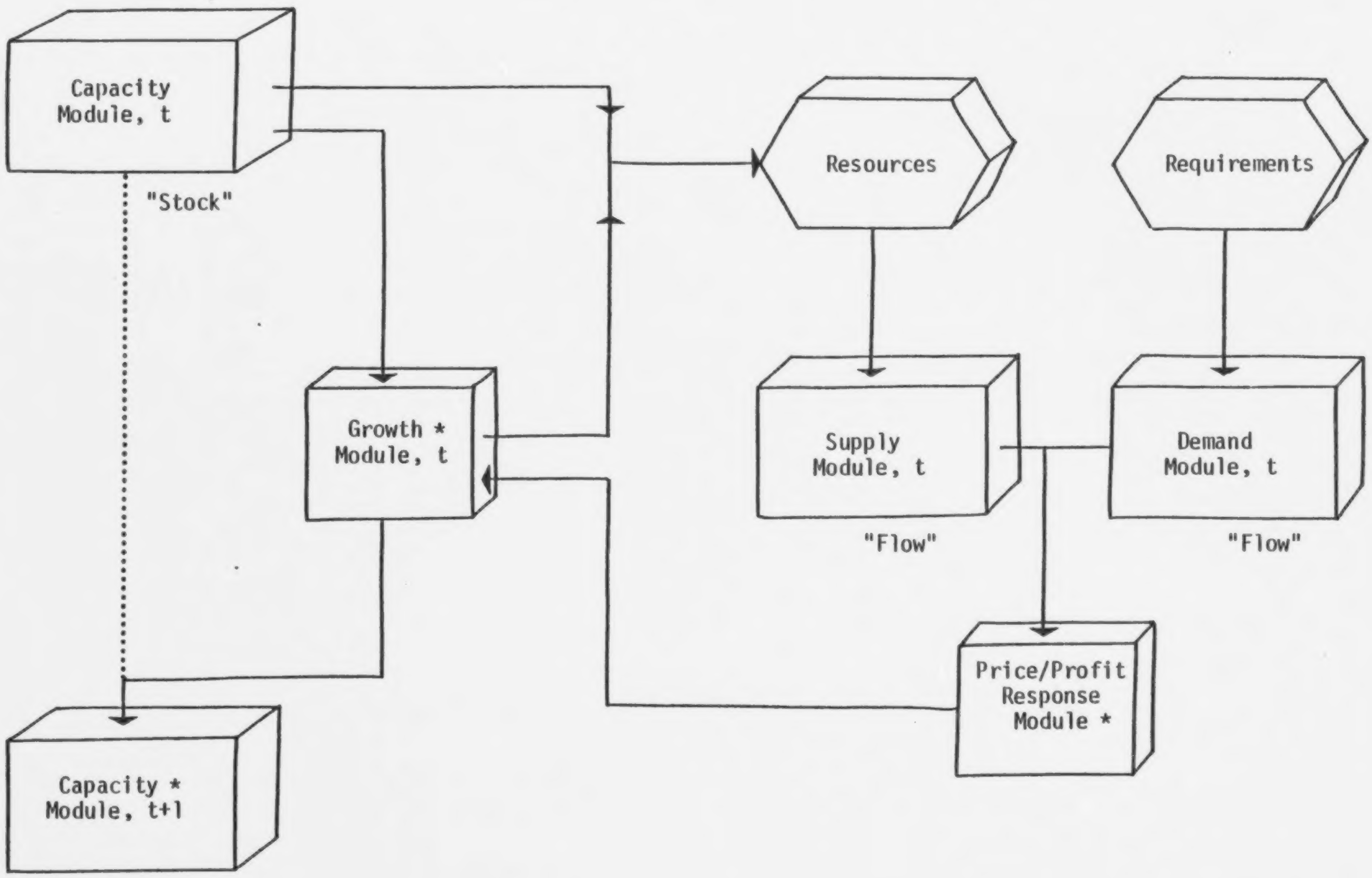
A. Analytical System

Exhibit V-1 depicts a conceptual analytical system that characterizes an economic profile of the chemical testing industry by segment and, theoretically, in the aggregate. In addition to showing the industry's conceptual supply and demand modules, the exhibit indicates the relationship between the industry's laboratory capacity from which its resources are drawn (stock concept) in order to generate current period supply (flow concept). This supply function concept (quantity of services offered at alternative price levels) can be reasonably expressed only in relation to capacity constraints that are currently applicable.

The indicated capacity module can be defined for a specified time period, t, although changes in capacity are possible within the "dynamic" testing service industry. Such changes, whether positive or negative, are conceptually represented by a growth module. Various economic forces will influence management decisions to expand or contract laboratory capacities and capabilities.

Major inputs into the growth module are the price and profit conditions reflected by short-term, supply-demand interrelationships. Such conditions, both in macroeconomic (industry) and microeconomic (firm) terms, are conceptually depicted in Exhibit V-1 as a price/profit response module. Such an analytical module is generally required to assess the dynamic aspects of the testing industry. (Static economic relationships

Exhibit V-1. Proposed analytical system, chemical testing industry study 1/


Capacity Module, t
"Stock"
Growth * Module, t
Resources
Requirements
Supply Module, t
"Flow"
Demand Module, t
"Flow"
Price/Profit Response Module *
Capacity * Module, t+1

1/ Components of the system to be applied to each major type of testing.

* These indicated modules are outside the scope of study, but they are essential elements of the overall system when viewed as a dynamic vs. a static system.

will be understood as a fixed period within a dynamic modeling framework; hence, the analytical system depicted includes basic linkages required for a dynamic, iterative analysis.)

Two other vital components in the proposed analytical system are: (1) the resources component of the supply model that is concurrently linked to the capacity and growth modules, and (2) the requirements component of the demand module. An essential condition of the analysis is to express units of testing supply and demand on a common basis and this appears to require that supply-resources and demand-requirements components be specified in comparable terms, e.g., personnel man-hours (by skill level), space, equipment hours (by type), animals, etc. Through the use of testing protocols or other estimating procedures, test demands must be converted into these basic requirements. Supplies of such resources can then "flow" from the capacity module. Generally, however, only those resources and requirements that are most limited or constraining need to be incorporated within the overall model.

A model design concept that expresses capacity, supply, and demand modules in common "units" is critical. Such units are the resources provided by suppliers of testing services and required by regulatory agencies to satisfy their testing rules. With this design concept, analysts ascertain whether sufficient resources are generally available to meet any specified set of test demands.

In general terms, this model should incorporate the following conditions:

Condition 1. Available capacity, C, during a given period t, must be greater than or equal to the supply, S, of testing services performed. Both C and S are expressed as functions of common resources R_k, where k denotes all applicable or key resources. That is,

$$C_t \geq S_t$$

where

$$C_t = f_t\ (R_1, R_2, \ldots, R_k, \ldots)$$

$$S_t = g_t\ (R_1, R_2, \ldots, R_k, \ldots)$$

Condition 2. Realized demand, D, for testing services during a given period, t, should equal supply, S, given Condition 1. D is also expressed as a function of common resources, R_k. That is,

$$D_t = S_t$$

where

$$D_t = h_t\ (R_1, R_2, \ldots, R_k, \ldots)$$

Condition 3. Specified capacities, supplies, and demands from alternate sources are to be aggregated (unless "submarkets" are uniquely defined for which separate analyses are then applicable). For example, C_t, S_t, and D_t are sets that will be aggregated as follows:

$$C_t = C_{1t} + C_{2t} + \dots + C_{it} + \dots$$

$$S_t = S_{1t} + S_{2t} + \dots + S_{it} + \dots$$

$$D_t = D_{1t} + D_{2t} + \dots + D_{jt} + \dots$$

where

C_t and S_t components C_{it} and S_{it}, are matched sets, and

D_t components D_{jt}, are distinct.

The above general conditions, which are detailed subsequently, must be satisfied within an operational system. One known operational approach is to specify a multi-equation model within a mathematical programming system. In a block-matrix context, the following equation-condition system is applicable:

	Vectors			Right Hand Side
	$C(\vec{X}_1)$	$S(\vec{X}_2)$	$D(\vec{X}_3)$	$(\vec{b})$
Capacity, C	A_{11}			$\vec{b}_1$
Supply, S		A_{22}		$\vec{b}_2$
C/S	A_{31}	A_{32}		$\vec{b}_3$
Demand, D			A_{43}	$\vec{b}_4$
S/D		A_{52}	A_{53}	$\vec{b}_5$

where

$$\begin{array}{lll}
A_{11}\overrightarrow{X_1} & = \overrightarrow{b_1} & (\overrightarrow{b_1} = \text{capacities}) \\
A_{22}\overrightarrow{X_2} & \geq 0 & (\overrightarrow{b_2} = \text{supplies}) \\
A_{31}\overrightarrow{X_1}+A_{32}\overrightarrow{X_2} & \geq 0 & (\overrightarrow{b_3} = \text{excess capacity}) \\
A_{43}\overrightarrow{X_3} & = \overrightarrow{b_4} & (\overrightarrow{b_4} = \text{demands}) \\
A_{52}\overrightarrow{X_2}+A_{53}\overrightarrow{X_3} & = 0 & (\overrightarrow{b_5} = \text{supply-demand=0})
\end{array}$$

The purpose of this equation system is to establish whether a "feasible" (vs. optimal) capacity, supply and demand set of conditions can be met. These capacity, supply and demand conditions determine whether the specified demand can be supplied (regardless of price) from available capacity. A subsequent equation system is needed to establish other supply-demand conditions and economic relationships.

Further specifications of the proposed model are presented in Sections D, E, and F. However, the supply and the demand modules of the overall model are first described in greater detail to introduce additional factors that should to be assessed.

B. Supply Module

The chemical testing industry is a service industry with a range of testing capabilities that may be utilized with limited flexibility in the short term. Specific toxicological tests generally require laboratory facilities that provide space, specialized equipment, uniquely trained personnel and other special resources (e.g., test animals and chemicals). To a degree, the maximum available supply of testing services is dependent on the mix of specific tests demanded because variable amounts of different key resources may be required. The concept of determining the most limiting special resource for any set of test demands can be employed to resolve this type of conflict, i.e., the "supply" is defined in terms of the most likely limiting resources during a given period of time, yet only one type will generally be the constraining, or key, resource for a given period of analysis.

Empirically, there are distinguishable supply sources of testing services: (1) independent laboratories, (2) captive laboratories, (3) university laboratories, (4) government laboratories, and (5) foreign laboratories. An element of concern to the analysis is that each source is not uniformly able to conduct specific chemical tests for commercial, private sector products. For example, government laboratories may be restricted from conducting product development-related testing. University laboratories may provide only limited and variable testing services. Foreign laboratories may be viewed as a competitive supply source or an auxiliary source if "excess demand" for testing arises. (In general, foreign laboratories' supply of resources are not assessed further in this study.)

Each of these sources has distinctive capacity (resource availability) and supply (resource use) characteristics. It is recommended that the capacity and supply modules of the model reflect each source separately as well as in the aggregate. In doing so, all sources' capacity and supply, individually and collectively, should be specified in common resource units.

Although each source's capacity and supply may be separately represented, another element of concern is that no provision has been made to identify from which supply source subsequent demands will be met. In other words, only an aggregate supply-demand interface is anticipated without the ability to uniquely link a given testing demand to a specific source of supply, S_i. Via network analysis principles, one can establish node-link conditions to assure that certain supply sources are utilized, if applicable. However, further study is required to determine whether such specifications are needed.

Another issue to resolve is that resource capacities from alternate sources may not be fully additive if they are not transferable or mobile. For example, excess personnel at one source (e.g., captive laboratory) may not be utilizable at another source (e.g. independent laboratory) should this resource be limiting at the latter source. Some physical resources, such as laboratory space, are not mobile; the mobility assumption would be very limiting in this case. However, unless otherwise developed, testing resources are presumed to be transferable within the system.

C. Demand Module

Aggregate toxicological testing demand can also be shown to stem from a variety of sources including both regulatory and nonregulatory testing. Within the regulatory category, the primary basis for organizing demand requirements is by Congressional or Executive agency act or by other regulatory authority. Thereafter, estimates must be made of the types of testing required and the specific amounts of testing to be conducted.

For example, the following Agencies and Acts provide a basis for categorizing testing demands, each of which can be modeled as a separate demand source:

Agency	Act
EPA	• TSCA • FIFRA • Other
FDA	• FFDCA • FHSA
OSHA	• OSHA
CPSC	• CPSA
USDA	• FAWA

Within each agency or act category, the types of testing required must be thoroughly assessed and test demands estimated (see Chapter IV). Furthermore, such demands need to be broken down into specific resource requirements within the demand module. Generally, the following hierarchy of testing requirements must be determined:

1. Chemical(s) to be tested
2. Specific tests (acute-subchronic-chronic)
3. Protocols (or estimated protocols)
4. Resource requirements (all modeled resources)

The latter resource requirements for all chemical substances and tests will represent the testing demand for each major source (agency or act). Exhibits IV-25 and IV-26 summarize the total number of tests for three sources--TSCA, FIFRA, FFDCA and the resources required for specified tests and protocols. These data, while preliminary, form a basis for modeling chemical testing demand.

The sum of all such regulatory demands (sum of all resource requirements) will represent the aggregate regulatory demand. Nonregulatory demands by both government and the private sector must also be determined and added to the regulatory requirements to determine total testing demand.

Nonregulatory testing demand is not well documented on an industry-wide basis; however, much of the previously "voluntary" toxicological testing may now be mandatory. Hence, the remaining nonregulatory testing may be comparatively minor. Even so, more effort is required to ascertain the sources and levels of testing (and the associated resource requirements) of nonregulatory demand. A component of this demand may be foreign testing demand that utilizes U.S. testing services.

As briefly indicated, all testing demands ultimately must be expressed in terms of their resource requirements. This will permit assessing the supply-demand resource balances and the utilization analysis of available capacities of resources from all sources.

An unresolved issue is the timing of testing demands and the associated resource requirements during a given period of analysis, e.g., year. Short-term testing requirements can be aggregated directly; however, long-term testing requirements must be allocated among the periods impacted with carry-over provisions for resource requirements that affect subsequent periods. Thus, "carry-in" requirements should also be assessed as well as any new testing demands.

D. An Accounting Subsystem

An accounting subsystem within the overall model is proposed to provide built-in capabilities for tracking resource-specific components of each of the analytical system's modules. As previously described, the capacity (C) and supply (S) modules are both expected to be source-dependent (independent laboratories, captive laboratories, etc.) as well as resource-specific. The demand (D) module is also source-dependent (TSCA, FIFRA, etc.) and resource-specific.

The purposes of an accounting subsystem include establishing resource-specific capacities of all supplying sources, simulating the flow of resources from the capacity module into the supply module, estimating resource-specific requirements by all sources of testing demand in the demand module, and equating resource-specific demand with supply subject to resource availabilities. In addition, these general accounting requirements will be subject to concurrent economic subsystem conditions which are described in Section E (although many of the proposed accounting features of the overall model are largely independent of subsequent economic specifications and constraints).

A more thorough specification of the capacity, supply and demand modules' variables and relationships follow. In particular, the accounting-type requirements of the overall model are shown.

Capacity, C, is characterized as the set (omitting subscript, t, for time which is implicit):

$$C = \{C_1, C_2, \ldots, C_i, \ldots\}$$

where

C = total capacity

C_i = capacity of source i for all applicable i

also,

$$C_i = f_i(R_{i1}, R_{i2}, \ldots, R_{ik}, \ldots)$$

where

R_{ik} = resource k from source i for all applicable k

f_i = functional relationship, general.

Toxicology laboratories comprising a given source i may alter their available resource levels under varying economic conditions. However, a static, beginning-of-the-period inventory-type measure of capacity is proposed, so that, also:

$$\overline{C}_i \equiv [\overline{R}_{i1}, \overline{R}_{i2}, \ldots, \overline{R}_{ik}, \ldots]$$

where

$\overline{C}_i$ = fixed, resource-specific capacity of source i for all applicable i

$\overline{R}_{ik}$ = the sum of all source i laboratories' available resource k (at the beginning of period t).

For this reason, capacity is said to be a stock concept (although the proposed growth module in Exhibit V-1 allows additions or deletions to be made to capacity). Also, capacity is a multi-variable concept because any number of resources, k, may be included, As noted, however, the major concern is to model critical or key resources, any one of which may be the constraining ("capacity-limiting") factor under alternate demand (or resource mix) conditions.

Another description of capacity, C, in this study's context, is that the resource values, $\overline{R}_{ik}$, represent the maximum values available from all applicable laboratories for each source i. (These are fixed values for a given period of analysis, t). All sources realized capacity may be further aggregated as follows:

$$C^r \equiv [\sum_i \overline{R}_{i1}, \sum_i \overline{R}_{i2}, \ldots, \sum_i \overline{R}_{ik}, \ldots]$$

where

C^r = realized total capacity for all sources i

$\sum_i \overline{R}_{ik}$ = sum of all source i's resource capacities for all applicable resources, k.

Supply, S, has general characteristics similar to capacity, C. However, the supply of toxicological services is operationally quite distinct. Supply, S, is also characterized as a set:

$$S = \{S_1, S_2, \ldots, S_i, \ldots\}$$

where

S = total supply

S_i = supply of source i for all applicable i
(Note: C_i and S_i are matched components for source i)

Also,

$$S_i = g_i(R_{i1}, R_{i2}, \ldots, R_{ik}, \ldots)$$

where

R_{ik} = resource k from source i for all applicable k

g_i = functional relationship, general.

The function, g_i, is conceptually complex and it represents the actual utilization of resources for conducting toxicological tests during a given period. This function does not explain how the supply is to be determined, rather it simply denotes that the supply of toxicological testing services consists of a collection of key resources from each source i. Differing combinations of resources may be supplied from each source (although no procedure is proposed herein to estimate each source's realized supply). An important accounting property, however, is that the aggregate supply, S, is presumed to be the sum of all utilized resources, k, across all sources i. In general notation the aggregate supply, S, is:

$$\begin{aligned} S &= g(\sum_i S_i) \\ &= g[\sum_i g_i(R_{i1}, R_{i2}, \ldots, R_{ik}, \ldots)] \end{aligned}$$

where

$\sum_i S_i$ = sum of all S_i (unspecified summation procedure)

g = functional relationship, general.

This general notation can be made more specific if there exists a unique "solution". For example, if supply equals demand during a given period, then a point on the general supply function, g, implicitly exists. Also, specific points on each source's supply function, g_i, exists. Thus, for such a case, the realized supply, S_i^r, can be defined in terms of the resources actually utilized. The aggregate realized supply, across all sources i, is defined as follows:

$$S^r \equiv [\sum_i R_{i1}, \sum_i R_{i2}, \ldots, \sum_i R_{ik}, \ldots]$$

where

S^r = realized supply (a specific value of the g supply function)

$\sum_i R_{ik}$ = sum of resources, k, utilized by all sources, i.

This supply estimate, S^r, is in the same form as the capacity estimate, C^r, above. Hence, the model condition that capacity be greater than or equal to supply can be assessed on a resource-specific basis.

The accounting requirements of the demand module are similar to the supply module in the aggregate because realized demand (resources required) must equal realized supply (resources provided) in "equilibrium"--an accounting condition. This condition will apply for each of the modeled resources.

Testing demand in economic terms is naturally expressed as a function of the tests that will be conducted on various chemicals under differing economic conditions. However, the following resource-specific demand equations are presented from an accounting subsystem perspective. These specifications, or definitions, are consistent with the economic subsystem although the economic rationale for them is indirect as is explained in the following pages of this section.

Demand, D, is the set:

$$D = \{D_1, D_2, \ldots, D_j, \ldots\}$$

where

D = total demand

D_j = demand from source j for all applicable j.

Also,

$$D_j = h_j(R_{j1}, R_{j2}, \ldots, R_{jk}, \ldots)$$

where

R_{jk} = resource k required by demand source j for all applicable k

h_j = functional relationship, general.

The function, h_j, generally indicates that each source j's demand will be expressed in terms of a common set of k resources. However, the level of demand, and the combination of resources required, may differ greatly among sources. In general terms, aggregate demand, D, is defined as follows:

$$D = h(\sum_j D_j)$$

$$= h[\sum_j h_j(R_{j1}, R_{j2}, \ldots, R_{jk}, \ldots)]$$

where

ΣD_j = sum of all demand source j's resource requirements for all resources k

h = functional relationship, general

Given a particular or realized demand level, for each source, there exists a set of k resource requirements that defines aggregate demand, D^r. That is,

$$D^r \equiv [\sum_j R_{j1}, \sum_j R_{j2}, \ldots, \sum_j R_{jk}, \ldots]$$

where

D^r = realized demand, (a specific value of the h demand function)

$\sum_j R_{jk}$ = sum of all source j's resource k requirements for all applicable k

In summary, these definitions of capacity, supply and demand will form an accounting subsystem framework where, ultimately, realized supply, S^r, will be equated with realized demand, D^r, subject to the condition that supply does not exceed the specified capacity, C^r, of any key resource.

$S^r = D^r$ (Equilibrium condition, applicable for all specified resources)

such that

$S^r \leq C^r$ (Capacity constraint)

A more elaborate specification of the demand resource requirements is needed in the model to track the toxicological testing demand process which is, generally, as follows:

Chemical → Tests → Protocols → Resource Requirements

As described in Chapter IV, a series of tests will usually be conducted for a given chemical--perhaps both regulatory and nonregulatory tests depending upon corporate and regulatory toxicological testing policies. Although specified tests may not be conducted in precisely the same manner for different chemicals, testing protocols are being developed or may be estimated for representative cases. Such estimated protocols are essential for simulating the demand, i.e., the resource requirements for various tests. Again, only major or critical resources such as pathologists, toxicologists, specified equipment, space, etc. may need to be simulated. Non-major resources such as laboratory supplies are presumed to be available in the quantities required and need not be (yet could be) embedded in the accounting subsystem.

A demand module accounting procedure is proposed as follows. Define a set of all possible tests, T, that may be used to assess the set of all expected chemical materials, M. (Either set may be expanded as required). That is, let

$$T = \{T_1, T_2, T_3, \ldots, T_m, \ldots\}$$

and

$$M = \{M_1, M_2, M_3, \ldots, M_n, \ldots\}$$

where

T = set of all tests possible

T_m = specific test m of set T

M = set of all materials expected

M_n = specific material n of set M.

Each test, T_m, is to have a specified and unique protocol, P_m, which minimally defines the level (see Exhibit IV-26) of all potentially critical resources that are required to perform the test. These resource requirements are denoted as follows:

$$P_m \equiv [\hat{R}_{1m}, \hat{R}_{2m}, \ldots, \hat{R}_{km}, \ldots]$$

where

P_m = protocol or resources required for test T_m

$\hat{R}_{km}$ = estimated amount of resource k required to perform protocol P_m.

Because each test, T_m, has a unique protocol, P_m, only the numbers of each test demanded by each source j is necessary to derive the associated and required toxicological testing resources. In particular, for each chemical material, M_n, all applicable tests must be determined by demand source, D_j. The number of each test required is summed for all chemical materials from that demand source. For example, the resource requirements of D_j can be indirectly expressed as the ordered set, N, of the number of each test required (or estimated):

$$N_j = (N_{j1}, N_{j2}, \ldots, N_{jm}, \ldots)$$

where

N_j = estimated total number of tests, or testing demand, from demand source j

N_{jm} = the number of test T_m required by demand source j.

As indicated above, since each test, T_m, has a unique protocol, P_m, this total demand for source D_j can now be converted into specific resource requirements. Further, the aggregate demand, D, from all sources can be derived by summing their tests ($\sum_j N_{jm}$) and their associated resource requirements.

A general procedure for incorporating these more detailed demand level resource requirements in the accounting subsystem of the model is outlined further in Section F. At this general development stage, the primary focus is on aggregate capacity, supply and demand conditions that must be satisfied according to economic expectations.

The following section discusses the economic subsystem of the overall model, including linkages to the accounting subsystem which will ensure that the resource specific conditions defined above will be satisfied along with subsequent economic conditions and objectives.

E. An Economic Subsystem

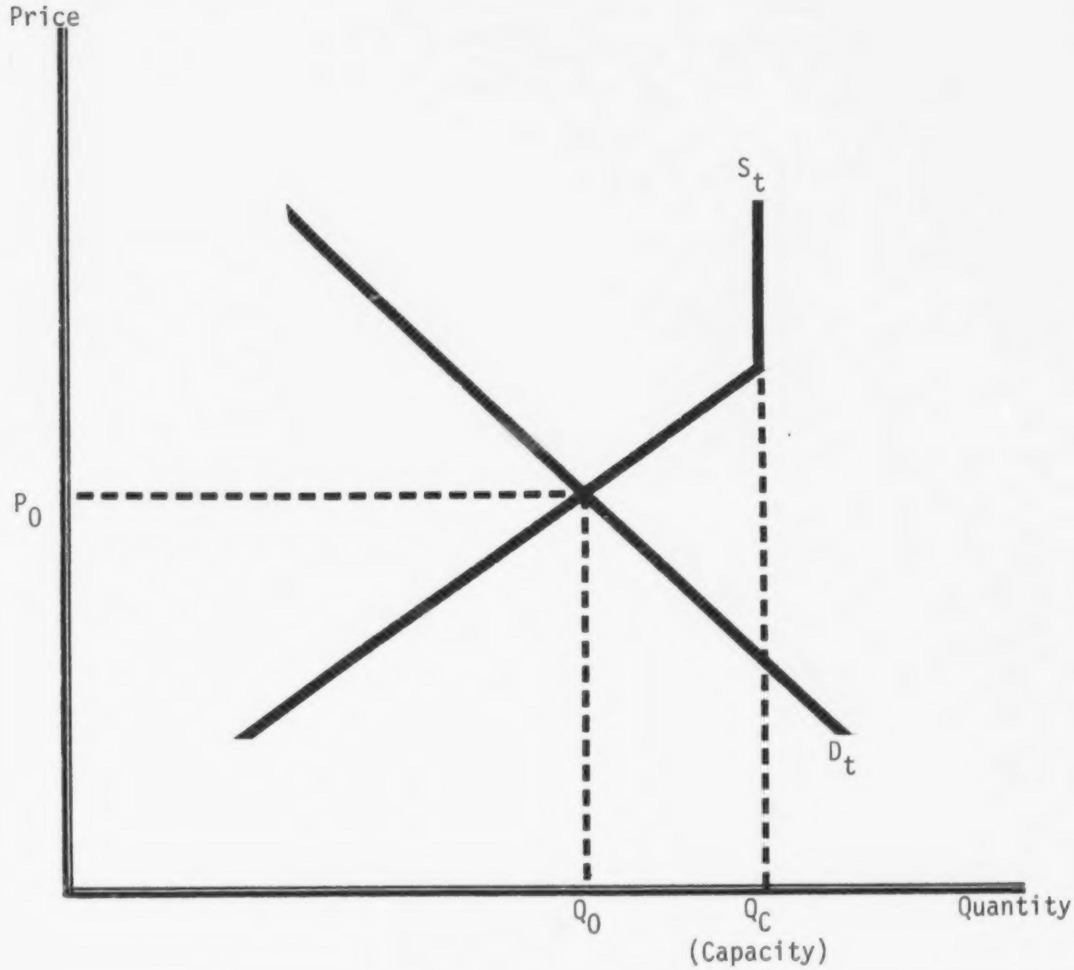
The preceding accounting subsystem provides one method for aggregating chemical testing resource units that are either supplied or demanded. This aggregation process can be completed for numerous supply sources (types of laboratories) and demand sources (agencies, acts and other). However, such an accounting procedure does not recognize the extremely variable economic conditions that affect both supply formation and demand generation processes. Ultimately, an economic subsystem is needed to simulate supply relationships by source and in the aggregate, and to simulate demand relationships by source and in the aggregate. As presented in Exhibit V-1, above, dynamic supply (capacity) and demand conditions are also relevant and can be introduced via the growth and the price-profit response modules of the proposed analytical system. Initially, however, static economic relationships should be developed in more detail.

Although simplified, theoretical toxicological testing supply, capacity and demand relationships may be depicted as shown in Exhibit V-2. For a given period, t, the supply, S_t, is shown to increase as a function of price up to a maximum quantity (capacity). Demand, D_t, is also a function of price but with a negative slope depicting higher quantities of testing with lower prices. A short-run equilibrium price-quantity point, (P_0, Q_0), is shown where the realized supply is also less than the capacity--a necessary condition.

A problem arises in interpreting "quantity" in this framework because various resources used in differing combinations for a variety of chemicals and tests are implied by the demand for (and supply of) toxicological tests. In practice, one can explicitly define all of the resources required to achieve the quantity, Q_0, but each alternate level Q might represent a different combination of resources. No problem exists in characterizing resource requirements, per se, so long as no limiting resource exists. Even then, the most limiting resource will determine the capacity to supply testing services, i.e., Q_c in Exhibit V-2.

The aggregate supply function depicted in Exhibit V-2 stems from alternate sources (e.g., independent, captive). Conceptually, the supply function for each source should first be estimated and then these functions summed

Exhibit V-2. Hypothetical chemical testing industry supply (and capacity) and demand functions for a given period, t



to simulate the aggregate chemical testing supply (and capacity). Also, each source's supply is theoretically the sum of the marginal cost curves for all firms in the industry segment. In practice, analysts typically evaluate only representative types and sizes of firms and then estimate intermediate and aggregate relationships from these cases. Major additional research is needed, however, to estimate the aggregate chemical testing industry supply by this method, i.e., from the micro (firm)-level to the aggregate level.

In the absence of such detailed supply estimates by source, only a grossly simplified aggregate supply estimate, such as portrayed in Exhibit V-2, is possible. For purposes of this conceptual discussion, the ability to estimate an aggregate supply (and capacity) function is presumed to exist.

The aggregate demand function depicted in Exhibit V-2 also represents multiple sources (e.g., agency, act and other). In theory, each source's demand function should be separately estimated and then all demand functions summed to simulate the aggregate-demand function as shown. This study partially estimated the quantity of testing required by selected agencies and acts as described in Chapter IV. The estimated number of tests required were not functionally related to the prospective prices of tests, however, and much additional research is needed to establish functional relationships for all sources of demand. Toxicological testing demand is derived from the prospective demand for the chemical products being developed as well as the cost of testing. Hence, this demand estimation process is complex. Again, in order to continue this conceptual discussion, the ability to estimate an aggregate demand function is presumed to exist.

At this stage, no attempt is made to characterize the mix of tests or resources that might be reflected by one-unit of the "quantity" of testing demand (and supply). However, given some unit of measurement (discussed further below), both the demand for and the supply of toxicological testing services should be defined as step-functions in a multi-equation model system where the economic subsystem can then be linked to the previous accounting subsystem. For example, the demand function could be expressed in terms of equal increments of demand (quantity of services) that are sought, but at consistently lower prices. The supply function could be expressed in terms of equal increments of supply (quantity of services) that are available only at increasingly higher prices (and until a constraining resource is encountered).

On the demand side, an initial procedure might be to simulate the completion of all testing requirements that are independently forecast by source of demand. Tests could be performed at "unit prices" (reflecting near minimum average total costs per test for representative laboratories or bid prices for tests per the protocol for each test. Implicitly, this demand function would be perfectly inelastic. If all tests can be feasibly conducted (without any resource capacity constraints), market prices may be near the estimated "unit prices". However, should resource constraints appear via the simulation (and excess demand appears in satisfying all accounting conditions) then adjustments in the supply and demand function should be made to forecast an equilibrium price and quantity.

The supply and demand functions should be estimated from both theoretical and empirical information. Previous market behavior data can aid in estimating whether wide price-cost margins arise during periods of shortages of toxicological capacity or whether cost subsidization occurs during periods of apparent surplus capacity. Also, microeconomic analysis of model firms can be conducted to estimate likely firm behavior based on economic theory. Numerous qualitative as well as quantitative factors influence firm decisions and aggregate market behavior.

In sum, these economic considerations should augment the accounting subsystem conditions as described in Section D. Procedures are needed to incorporate into the overall model those applicable supply response and demand behavior conditions while maintaining the previously described accounting subsystem conditions.

The above general analytical approach can be readily implemented using available mathematical programming and network analysis techniques. However, additional theoretical and empirical research is necessary before reasonably accurate supply and demand prices can be associated with the proposed equal increments of the "quantity of services".

Two additional model development concepts are critical: (1) specifying an objective function for predicting supply-demand behavior, and (2) simulating likely behavior in the chemical testing industry over a limited price-quantity range. First, to implement the model, some type of decision algorithm or objective function is required to predict behavioral responses. For example, in Exhibit V-2, one can readily infer that the point (P_0, Q_0) is an equilibrium point where demanders' "willingness to pay" equals suppliers' prices, and the suppliers' capacity is not exceeded. But such functions, are unknown, a priori. This same equilibrium point might be simulated in a different manner, however. One approach is to specify an objective function that "adds" incremental units of testing demand (quantity of services), at minimum cost, so long as the demand price is greater than or equal to the supply price--and the supply capacity is not exceeded. A mathematical programming system can readily simulate such a solution.

The second concept involves a concentration of research effort within a pertinent range around the expected equilibrium point in the simulations. Again referring to Exhibit V-2, analysts will seldom be highly interested in supply or demand levels and prices that are very distant from the equilibrium values. This does not preclude the assessment of a wide range of quantities or prices that may be caused by major shifts in supply demand. Rather, the analysis should generally concentrate on "finding" initial equilibrium values and then assessing likely deviations therefrom due to changes in economic conditions.

An earlier suggestion for estimating an initial solution (after which a range of supply-demand price and quantity values might be assessed) was to presume the demand function is perfectly inelastic (vertical in Exhibit V-2). This would facilitate determining whether projected demands could be met with available resources (less than or equal to capacity). In such a simulation, a step-function supply relationship, with rising costs for additional increments of supply, could be used. The primary purpose for such a simulation would be to find an approximate equilibrium value and establish a range of prices and quantities over which more accurately specified demand and supply step-functions could be modeled and assessed.

Since various implementation approaches are possible, no exact procedure is proposed. However, the following economic subsystem conditions and constraints are essential:

1. Simulate a supply function. A step-function approach is proposed where increments of supply are "available" at increasingly higher prices (up to the capacity constraint as defined in the accounting subsystem). Ideally, the aggregate supply will be estimated from more detailed analysis of each supply source.

2. Simulate a demand function. Aggregate testing demand from all sources might also be simulated using a step-function approach. In this case, increments of demand are added but at consistently lower prices (willingness to pay). Characteristics of each demand source (market) should be known in developing such an aggregate demand.

3. Specify an objective function (decision algorithm). A common objective function in a mathematical programming system is to satisfy requirements (demand) at minimum cost (price) while also meeting other conditions/constraints. The minimum cost of incremental resources is reflected in the supply function. In this model, the proposed objective function is to maximize the sum of the differences between the demand price, P_d, and the supply cost, C_s, over all levels of testing demand and supply (i.e. maximize the sum of consumer's and producer's surplus).

4. Other conditions. The suggested step-function approach (both supply and demand) requires that the last increment of supply be added so long as the "demand price" (associated with a corresponding increment of demand) is greater than or equal to the "supply price". This economic condition must be incorporated in the model. An illustration of this type of constraint is included in Section F.

These economic subsystem constraints and conditions are suggested to apply in the aggregate, i.e., for all supply sources and for all demand sources. Unique supply and demand functions for each applicable source are desired and they can be summed to derive aggregate relationships. Also, model linkages among specific supply and demand sources can be developed if applicable. These conditions are not illustrated, however.

F. General Implementation Requirements

While this study's scope of work does not include implementing the proposed conceptual model, several methodological steps are suggested below. As described above, the conceptual model development presumes that source-dependent demands and supplies can be estimated and aggregated. Such estimates will be difficult to obtain. A further complication is that some common unit of testing service ("quantity") is required for each source separately and in the aggregate. This requirement is generally too strict in an overall sense, but if a "near-equilibrium" solution could be simulated, then the same "mix of resources" could serve as a proxy unit of supply and demand, e.g., a unit might be one veterinary pathologist plus the average amount of space, equipment, animals, etc. associated with this resource. Step-function changes in supply and demand could be simulated thereafter. Prospective shifts in demand induced by TSCA might then be characterized in this unit of analysis and evaluated.

Another basic approach, after simulating a baseline, short-term equilibrium is to forecast TSCA-related incremental demand and to determine whether such testing demand (required resources via protocols) can be supplied from the remaining resource capacities, regardless of their supply source. This approach would focus on the accounting subsystem conditions, however, and not reflect probable "price" increases because of shifts along the industry's supply function.

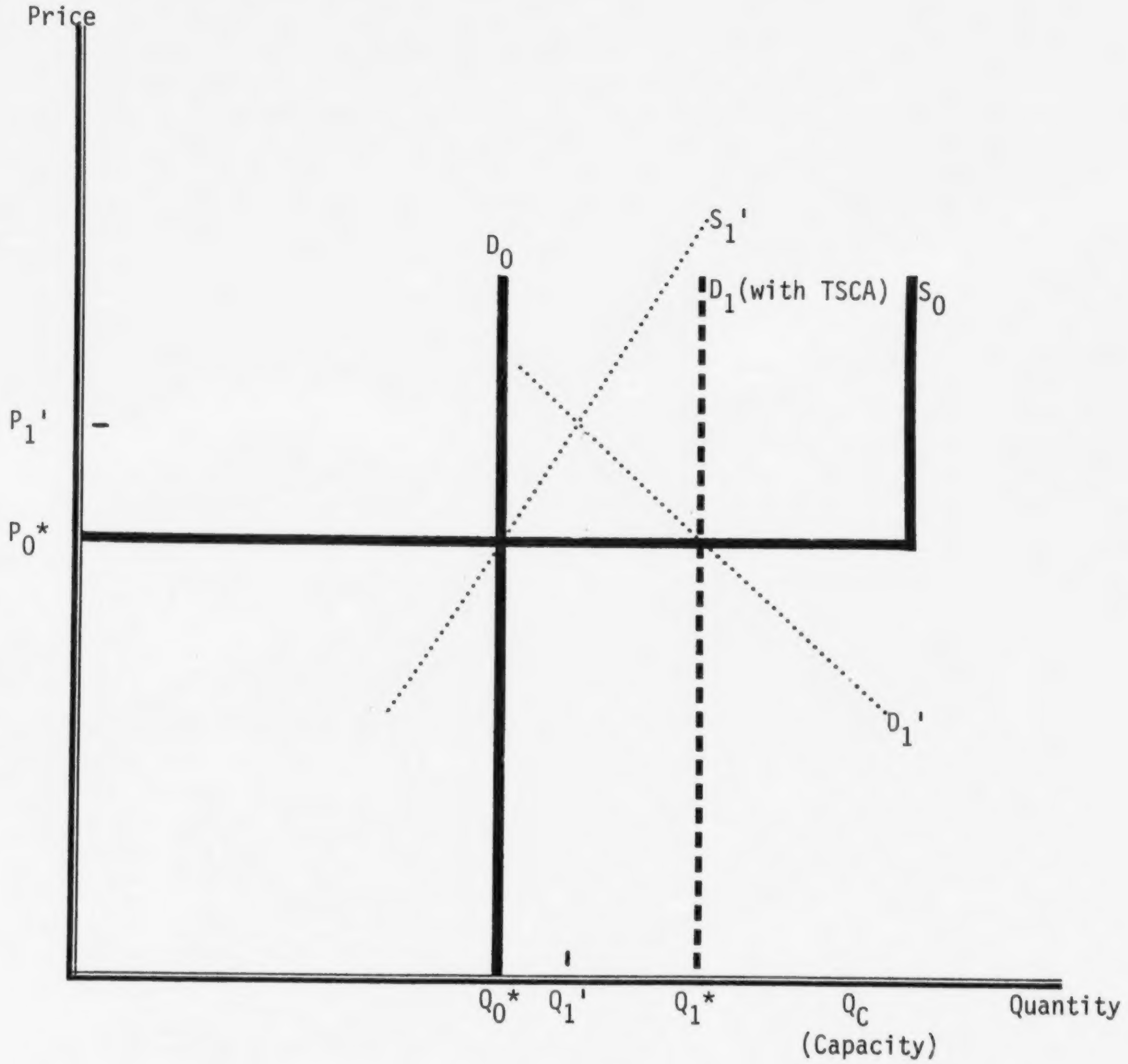
This latter approach is similar to presuming that the aggregate supply function is perfectly elastic (up to the first constraining resource level) and the demand function is perfectly inelastic as depicted in Exhibit V-3. In this graph an assumed initial equilibrium "price" and "quantity" level, (P_0^*, Q_0^*), is defined, but no further price effect will occur until the capacity of the most limiting resource is reached. Then, price is indeterminant. In contrast, the with-TSCA demand shift, D_1, is expected to result in a new equilibrium higher price, P_1', and quantity, Q_1', between Q_0^* and Q_1^*, as depicted.

The conditions set-forth in the accounting subsystem section above are effectively represented by the solid-line demand and supply functions in Exhibit V-3, i.e., the perfectly elastic supply and the perfectly inelastic demand assumptions.

The primary goal of the economic subsystem is to more closely reflect actual supply-demand conditions either in the aggregate or by source of supply and demand. This goal should be accomplished while maintaining the accounting subsystem conditions. Hence, at least some degree of improvement in estimating price levels and quantity levels of testing is expected.

An illustration of the previously described accounting and economic subsystems' conditions within a mathematical programming framework is shown in Exhibit V-4. This illustration is simplified by limiting the number of

Exhibit V-3. Potential chemical testing industry supply and demand functions, accounting vs. economic concepts



[Note: S_1' and D_1' represent theoretically expected supply and demand functions--see Exhibit V-2. Expected equilibrium equals (P_1', Q_1') versus (P_0*, Q_1*) with incremental TSCA demand to D_1.]

Exhibit V-4. Preliminary matrix specification of a mathematical programming model of the chemical testing industry

Activity		Capacity						Supply						Demand						Resources required						Excess demand		Step Functions 1/				Condition	Right Hand Side
		C1		C2		C		S1		S2		S		D1		D2		D		T1		T2		T				Supply		Demand			
Condition		R1	R2	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2	T1	T2	T1	T2	T1	T2	R1	R2	R1	R2	R1	R2	R1	R2	ΔS1 (c1)	ΔS2 (c2)	ΔD1 (p1)	ΔD2 (p2)		
1. Capacity																																	
C1	R1	1																														=	$\overline{R}11$
	R2		1																													=	$\overline{R}12$
C2	R1			1																												=	$\overline{R}21$
	R2				1																											=	$\overline{R}22$
C	R1	-1		-1		1																										=	0
	R2		-1		-1		1																									=	0
2. Supply																																	
S1	R1							1																								≥	0
	R2								1																							≥	0
S2	R1									1																						≥	0
	R2										1																					≥	0
S	R1							-1		-1		1																				=	0
	R2								-1		-1		1																			=	0
3. Capacity/Supply																																	
C/S	R1					1						-1																				≥	0
	R2						1						-1																			≥	0
4. Demand																																	
D1	T1													1																		≤	N11
	T2														1																	≤	N12
D2	T1															1																≤	N21
	T2																1															≤	N22
D	T1													-1		-1		1														=	0
	T2														-1		-1		1													=	0
5. Resources (Test Protocols) 2/																																	
T1	R1																	(a1)		-1												=	0
	R2																	(b1)			-1											=	0
T2	R1																		(a2)			-1										=	0
	R2																		(b2)				-1									=	0
T	R1																			-1		-1		1		(1) 3/						=	0
	R2																				-1		-1		1		(1)					=	0
6. Supply/Demand (Equality)																																	
S/D	R1											1												-1								=	0
	R2												1												-1							=	0
7. Step Functions																																	
S(R1)	S (Supply)											1																-1	-1			=	0
	ΔS1																											1				≤	ΔS1
	ΔS2																												1			≤	ΔS2
D(R1)	D (Demand)																							1						-1	-1	=	0
	ΔD1																													1		≤	ΔD1
	ΔD2																														1	≤	ΔD2

1/ The supply function costs, c_s, per interval, ΔS_s and the demand function prices, p_d, per interval, ΔD_d may be used in the model's objective function to maximize the sum of the differences between the demand prices and the supply costs, i.e., continue testing, subject to model conditions so long as $p_d \geq c_s$, i.e. max Σ $(p_d - c_s)$ over all intervals. These functions are expressed here in terms of a single resource, R_1, but a specified mix of resources could be modeled.

2/ Test protocals are to be expressed in units of each potentially constraining resource. Only two general resources, R_1 and R_2, are shown for illustration.

3/ Excess demand is a slack activity always ≥ 0 that would enter the solution only if the capacity of one or more resources was exceeded. This specification allows the problem to be solved but the solution is invalid as will be known by the Excess Demand column solution of the model. The amount of excess demand for each resource will be denoted.

supply and demand sources to two each. Also, only two tests with two resources are incorporated within the model. Actual implementation of such a system could be readily expanded to simulate numerous sources, tests and resources, as applicable.

As a guide to interpreting the activities and conditions of the matrix formulation of the model, the following definitions will apply (based on preceding descriptions of variables):

Capacity

- $C = \{C_1, C_2\}$

  where

  C = total capacity (maximum available resources) from all applicable sources i

  C_i = capacity of source i, i = 1, 2.

- $\overline{C}_i \equiv [\overline{R}_{i1}, \overline{R}_{i2}]$ (For a specific period of time, t.)

  where

  $\overline{C}_i$ = specified resource capacities for source i (for all applicable resources k)

  $\overline{R}_{ik}$ = maximum available amount of resource k from source i, k = 1, 2.

Supply

- $S = \{S_1, S_2\}$

  where

  S = total supply of testing resources

  S_i = supply of testing resources from source i, i = 1, 2.

- $S^r \equiv [\sum_i R_{i1}, \sum_i R_{i2}]$ (To be determined with the model)

  where

  S^r = realized supply of testing resources for all applicable sources i, i = 1, 2.

  ΣR_{ik} = sum of each resource k utilized by all sources i, k = 1, 2.

Demand

- $D = \{D_1, D_2\}$

  where

  D = total demand for testing resources

  D_j = demand for testing resources from source j, $j = 1, 2$.

- $D^r \equiv [\Sigma R_{j1}, \Sigma R_{j2}]$ (To be determined with the model)

  where

  D^r = realized demand for testing resources for all applicable sources j, $j = 1, 2$

  $\Sigma_j R_{jk}$ = sum of each resource k required by each demand source j, $k = 1, 2$.

Tests (and Protocols)

- $T = \{T_1, T_2\}$

  where

  T = the set of all possible tests that may be demanded by all demand sources j, $j = 1, 2$.

  T_m = test m of the set, $m = 1, 2$.

- T_m may be conducted and specified any number of times on any applicable chemical material by all applicable demand sources. However, a unique and specified protocol, P_m, will determine the amount of resources required. That is, $P_m \equiv [\hat{R}_{1m}, \hat{R}_{2m}]$, where $\hat{R}_{km}$ is the amount of resource k required to conduct the test, T_m. In particular, for this example, $P_1 \equiv [a_1, b_1]$ and $P_2 \equiv [a_2, b_2]$.

- $N_j = (N_{j1}, N_{j2})$ (To be input into the model)

  where

  N_j = estimated total number of tests, or testing demand, from all applicable demand sources j, $j = 1, 2$.

  N_{jm} = the number of test T_m required by demand source j, $m = 1, 2$.

Resources

- Resource requirements to meet a given demand by source (and in the aggregate) can be calculated with the preceding variables. For example, for demand source j, the total resource requirements are estimated as follows:

  (1) Test 1: $N_{j1} \times \hat{R}_{11} = R_{j1}$ requirement

  $N_{j1} \times \hat{R}_{21} = R_{j2}$ requirement

  (2) Test 2: $N_{j2} \times \hat{R}_{12} = R_{j1}$ requirement

  $N_{j2} \times \hat{R}_{22} = R_{j2}$ requirement

  These resource requirements, by test, are to be added for each resource k, k = 1, 2 to obtain each source j's resource demands. Further, the aggregate requirements for each resource k are obtained by summing over all sources j, j = 1, 2.

- The accounting subsystem of the proposed system will track and sum all applicable resource demands (and supplies) given the defined variables.

Step Functions

- Supply $S = (\Delta S_1 + \Delta S_2)$

  where

  Supply S = a step function approximation of $S = g(\sum_i S_i)$ above

  ΔS_s = increment s of total supply where each increment has a unique supply cost, c_s, that is increasing in value for each added increment

- Demand $D = (\Delta D_1 + \Delta D_2)$

  where

  Demand D = a step function approximation of $D = h\ (\sum_j D_j)$ above

  ΔD_d = increment of total demand where each increment has a unique demand price, p_d, that is decreasing in value for each added increment

- These functions are expressed in terms of a single resource, R_1, as shown in Exhibit V-4. However, a specified mix of resources could be the unit of analysis.

Given these definitions, the following accounting and economic subsystem conditions are embedded in the proposed model.

1. Capacity--the maximum available resources from each source are specified as right hand side (RHS) values, i.e., $\overline{R}_{ik}$. Also, these resources are accumulated for all sources, i.e., $\sum_i \overline{R}_{ik}$, for each k.

2. Supply--each source's supply of resources must be greater than or equal to zero (RHS condition). These resources are aggregated, i.e., $\sum_i R_{ik}$, for each k. Two linkages are also involved: capacity-supply, and supply-demand equality as described below.

3. Capacity-Supply--the condition in which capacity is greater than or equal to the supply (of each resource) is specified, i.e., $C^r - S^r \geq 0$.

4. Demand--demand is characterized as the number, N_{jm}, of each test, T_m, that is projected to be required by each demand source j. These requirements are specified as RHS values. Also, the total number of each test required by all demand sources is accumulated. (A less than or equal RHS condition denotes that all tests may not be conducted subject to the objective function economic criteria discussed below.)

5. Resources (Test Protocols)--each test has a specific amount of each major resource that is required to complete the test per a test protocol. For example, $P_1 = [a_1, b_1]$ and $P_2 = [a_2, b_2]$. These resource coefficients are specified for each test as column vectors in Exhibit V-4. The amount of each resource required for all tests is aggregated within the system, e.g., a_1 and a_2 relate to R_1 and b_1 and b_2 relate to R_2.

6. Supply-Demand Equality--a necessary accounting condition is that supply equal demand, i.e., all resources required (demanded) must be obtained from the capacity of resources available (supplied). This condition can be met unless the capacity of any one resource is exceeded, i.e., excess demand. A mathematical programming convention is to allow for this occurrence by introducing a slack activity which denotes a "problem", but which allows the supply-demand equality condition to be technically satisfied.

7. Excess Demand--as indicated in 6, slack activities for each resource, R_1 and R_2, are incorporated in the model. Should either of these column vectors, or both, enter the final programming solution, then an excess demand for the resource(s) exist. The amount of excess demand will be determined.

8. Step Functions--both the supply and the demand estimates can be programmed as incremental, step functions. As defined above, Supply S = $(\Delta S_1 + \Delta S_2)$ and Demand D = $(\Delta D_1 + \Delta D_2)$. Also, supply costs, c_s, and demand prices, p_d, are specified for each increment. The amounts of testing supply and demand (each expressed in terms of R_1 only) are specified as RHS values and conditioned to be less than or equal to the specified amounts. This condition does not require that all increments be supplied or demanded (subject to the objective function of the problem).

9. Objective Function--an ultimate goal of this type of model is to simulate industry behavior. While much further development is required, an initial simulation, using the objective function of a mathematical programming system, is to maximize the sum $(p_d - c_s)$ over all increments of demand and supply. In this situation, if the supply cost, c_s, increases (or the demand price, p_d, decreases) and is greater than p_d, then all tests would not be conducted because of economic conditions. The solution obtained would, in economic terms, maximize the sum of consumer's and producer's surplus.

   A much more elaborate price-profit response module is preferred when simulating industry behavior. However, the type of model proposed can be effective in characterizing and assessing aggregate industry behavior.

G. Research Implications

The implementation of a comprehensive supply-demand model of the toxicological testing industry, will require substantially more industry data than are presently available. More detailed supply data (resources) are required to implement the proposed model and an extension of the toxicology laboratory survey (see Chapter III) is recommended as a practical means for estimating resource capacities, testing capabilities, and related economic characteristics of the toxicological testing industry.

More detailed demand data (chemicals, tests and their resource requirements) are also required to implement the proposed model. As discussed earlier in this report (see Chapter IV), anticipated testing demands are much more difficult to estimate. Regulatory agencies can require that certain types of chemicals be tested for their toxicological effects, but the number of chemicals that will actually be introduced by chemical developers is generally unknown. Simple trend extrapolations of past testing (concerning the number of chemicals introduced and the profile of tests required or actually conducted) are perhaps useful, but not explanatory. Overall, a much greater research effort is necessary to improve toxicological testing demand estimates and to incorporate such estimates in the proposed model.

More specific implications of this research are discussed below.

1. Supply and Capacity

Two sources of testing supply provide the majority of the capacity for commercial toxicological testing--independent laboratories and captive (company) laboratories. These sources need to be better documented in terms of their toxicological testing capabilities and capacities, i.e., key resources. This study's laboratory survey (see Appendix B) provided some of the needed information but more detailed data are preferred.

Data obtained via the survey allow analysts to broadly estimate the total industry testing capacity, the current utilization of that capacity for present regulatory and non-regulatory demands, and, thus, the potential capacity available for use in testing chemicals under Section 4 of TSCA.

The information obtained from the survey also provides for a general economic assessment of the present industry. Problems remain, however, in in translating the information into a resource-specific form useful for the model. These data are useful in assessing the industry for a particular point in time, but changes occurring over the short and longer term need to be estimated if the model is to be an accurate tool for regulatory officials. The survey information is most helpful in developing the accounting subsystem of the model and in determinating the industry's present supply (and capacity) in terms of testing capabilities and resources. A more extensive survey of the industry's toxicology laboratories could provide detailed supply and capacity data for the model.

Two other chemical testing sources are university and government laboratories. These supply sources provide limited commercial testing services, which should be modeled, but more importantly, they compete for personnel and other key resources. Hence, for both reasons, the capacities and capabilities of these sources need further study. Foreign laboratories, as well, are potential suppliers of chemical testing services; their potential supply source capability and capacity should be assessed in greater detail.

2. Demand

A major effort was made in this study to estimate both regulatory and nonregulatory toxicological testing demand as discussed in Chapter IV. Many assumptions and estimates were necessary to forecast expected testing levels (chemicals, tests, protocols, and resources). Improved forecasts are needed and possible, but only with much additional research. Regulatory agencies such as FDA and EPA have extensive data bases that might be analyzed further to estimate testing demands.

Chemical developers (companies) conduct many toxicological tests either for research (before regulatory testing) or for nonregulatory reasons. These testing demands were not well documented with available data, and a better analysis of such testing demands is needed. The timing of research and nonregulatory testing is apparently affected substantially by competing regulatory requirements. This type of industry behavior needs to be better understood. Modeling efforts, especially the dynamic aspects of toxicological testing, should be tailored accordingly to better estimate continuing or multi-period testing demands for each period of analysis. Uncertainties of the timing of regulations and their protocols also contribute to irregular demand levels.

3. Prices and Other Factors

Prices for toxicological tests are a difficult to assess. Wide variability exists in quoted prices for similar tests. Part of this variability stems from differences in test protocols, but quality and other factors (e.g., ability to provide legal representation) apparently affect prices markedly. If traditional supply-demand economic models are to be used successfully, further studies need to be made of price-profit mechanisms within the industry.

The toxicological testing segment of the chemical testing industry has experienced rapid changes in the recent past, e.g., 1976-1981. Both independent and captive laboratories have been built and existing facilities have been expanded. In general, economic conditions in the industry have been unstable--largely because of uncertainties surrounding regulatory programs, including TSCA, FIFRA, and FFDCA. While these recent changes complicate economic analyses--with or without a model--they also exemplify the need to develop a better understanding of the chemical testing industry.

In conclusion, this study represents an initial effort to establish an economic profile of the toxicological testing segment of the chemical testing industry. The supply and demand characteristics of the industry are documented to the extent possible based upon secondary data and this study's relatively brief telephone survey of toxicology laboratories. Additionally, the study developed a supply-demand model capable of being implemented. Many research tasks remain before a comprehensive economic profile is established and an economic supply-demand model of the industry can be implemented, but these tasks are realistically attainable. Provided that a model is not implemented in the near future, a survey of toxicology laboratories, like the one conducted successfully for this study, might be repeated periodically. Such a survey documents the status of this dynamic industry and periodic surveys would disclose important economic characteristics regarding the availability and adequacy of toxicological testing services in the U.S.

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APPENDIX A

LISTING OF TOXICOLOGICAL TESTING LABORATORIES

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LISTING OF TOXICOLOGICAL TESTING LABORATORIES

The following listing contains 272 laboratories that have indicated toxicological testing capabilities. The list stems from a telephone survey of a screening list containing 800 potential toxicology laboratories and represents the laboratory's own designation as a toxicology laboratory. The screening list was compiled primarily from numerous directories and lists of laboratories; these sources are identified on the next page. Other laboratories for the screening list were obtained from trade journals and magazines and from referrals by surveyed laboratories.

The study and screening list was oriented toward laboratories providing commercial testing, either in-house or contract, and thus some university (teaching and research) laboratories and government laboratories were excluded. Due to a lack of information and study constraints, foreign laboratories also were excluded.

The final listing is not comprehensive even for commercial testing laboratories, as several factors prevented reaching this goal. Directories and listings were somewhat out-dated and none was comprehensive. During the survey, time was not sufficient to thoroughly investigate potential laboratories not answering telephones or with telephone numbers no longer in service (these laboratories were assumed to be out-of-business). Most new laboratories were included only through referrals and some probably were not identified. Still it is the study team's judgment that the list provides excellent coverage of the industry and only about 10 to 20 laboratories exclusions are estimated, bringing the total number of laboratories providing commercial toxicological testing to about 280 to 290 or, for analytical purposes, an estimated 285.

The listing contains the following types of laboratory information (unless unavailable):

- Name
- Address
- Contact Person (survey respondent)
- Phone

While the survey provided additional information on most of the laboratories, this information was not included to avoid individual laboratory concerns about confidentiality of the survey.

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CTT/80	Chemical Times & Trends, 1980 Directory of Toxicology Testing Laboratories
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SOT/76	Society of Toxicology, Toxicology Laboratory Survey, Mar. 1980
TR/1980	Thomas Register, 1980. New York: Thomas Publishing Co.

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

1 ABBOTT LABORATORIES
1400 SHERIDAN LN.
N.CHICAGO IL 60054
PHONE: 312/937-5763
CONTACT: DR. KESTERSON

2 AER-AQUA LABORATORIES INC.
P O BOX 18615
HOUSTON TX 77023
PHONE: 713/923-4885
CONTACT:

3 ALLERGAN PHARMACEUTICALS/HERBERT LABORATORIES
2525 DUPONT DR.
IRVINE CA 92713
PHONE: 714/752-7400
CONTACT: FRANK KILLEY

4 ALLIED ANALYTICAL AND RESEARCH LABORATORIES
3031 GLENFIELD
DALLAS TX 75224
PHONE: 214/337-8996
CONTACT: MORRIS WELLER

5 ALLIED CHEMICAL CORP./CHEMICAL RESEARCH CENTER
P O BOX 1057R
MORRISTOWN NJ 07960
PHONE: 201/455-2000
CONTACT: DR. REINHOLD

6 ALLIED LABORATORIES, LTD.
7011 HIGGINS AVE.
CHICAGO IL 60656
PHONE: 312/631-1553
CONTACT: DR. IRVING DOMSKY

7 AMERICAN BACTERIOLOGICAL & CHEMICAL RESEARCH CORP.
3437 SOUTHEAST 24TH AVE.
GAINESVILLE FL 32601
PHONE: 904/372-0436
CONTACT: MR. B. BORDEAUX

8 AMERICAN CYANAMID
QUACKERBRIDGE RD.
WEST WINDSOR NJ
PHONE: 609/799-0400
CONTACT: DR. DEEMS

9 AMERICAN CYANAMID CO. LEDERLE LABORATORIES
N. MIDDLETOWN RD.
PEARL RIVER NY 10965
PHONE: 914/735-5000
CONTACT: DR. JOHN NOBLE

10 AMERICAN HEALTH FOUNDATION NAYLOR DANA INSTITUTE
DANA RD.
VALHALLA NY 10595
PHONE: 914/592-2600
CONTACT: DR. SHIMADI

11 AMERICAN HOSPITAL SUPPLY CORP. EDWARDS LABORATORIES DIV.
17221 RED HILL AVE.
SANTA ANA CA 92705
PHONE: 714/557-8910
CONTACT: JOANNE FARLEY

12 AMERICAN HOSPITAL SUPPLY CORP. MCGAW LABORATORIES DIV.
2525 MCGAW AVE.
IRVINE CA 92650
PHONE: 714/754-2000
CONTACT: DR. ASHBROCK

13 AMERICAN STANDARDS TESTING BUREAU, INC.
40 WATER ST.
NY NY 10004
PHONE: 212/943-3156
CONTACT:

14 AMOCO CHEMICAL CORP.
200 E. RANDOLPH DR.
CHICAGO IL 60601
PHONE: 312/856-5991
CONTACT: DR. GARVIN

15 AMR BIOLOGICAL RESEARCH
690 SOUTH CLINTON
TRENTON NJ 08611
PHONE: 609/695-7700
CONTACT: DR. S. MARGOLIN

16 AMWAY CORP./RESEARCH & DEVELOPMENT DIV.
7575 E. FULTON RD.
ADA MI 49355
PHONE: 616/676-6279
CONTACT: SUE USHER

17 ANALYTIC AND BIOLOGICAL LABORATORIES INC.
10754 FORD RD.
GARDEN CITY MI 48135
PHONE: 313/422-7474
CONTACT: F. MCLAUGHLIN

18 ANALYTICAL BIO-CHEMISTRY LABORATORIES INC.
P O BOX 1097
COLUMBIA MO 65201
PHONE: 314/474-8579
CONTACT: MR. LYLE JOHNSON

19 ANALYTICAL CENTER INC.
P O BOX 15635 6001 CLINTON DR.
HOUSTON TX 77020
PHONE: 713/676-0141
CONTACT: B. SEASE

20 ANALYTICAL RESEARCH LABORATORIES INC.
160 TAYLOR ST.
MONROVIA CA 91016
PHONE: 213/357-3247
CONTACT: RAYMOND JAY

21 APPLIED BIOLOGICAL SCIENCES LABORATORIES INC.
6320 SAN FERNANDO RD.
GLENDALE CA 91201
PHONE: 213/242-6944
CONTACT: DR. J. B. MICHAELSON

22 APPLIED RESEARCH LABORATORIES OF FLORIDA INC.
650 PALM AVE.
HIALEAH FL 33010
PHONE: 305/245-3660
CONTACT: DR. STEWART

23 AQUALABS INC.
2221 HANCOCK DR.
AUSTIN TX 78756
PHONE: 512/453-3508
CONTACT: M. EDGAR

24 ARGUS RESEARCH LABORATORIES
2025 RIDGE RD.
PERKASIE PA 18944
PHONE: 215/257-2741
CONTACT: MR. ALLEN HOBERMAN

25 ARMOUR RESEARCH LABORATORY
15101 N. SCOTTSDALE RD.
SCOTTSDALE AZ 85260
PHONE: 602/991-3000
CONTACT: HELEN NORTA-ROOT

26 ARTHUR D. LITTLE INC.
ACORN PARK
CAMBRIDGE MA 02140
PHONE: 617/864-5770
CONTACT: DR. ANDERSON

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

27 ASSOCIATED WATER AND AIR RESOURCES ENGINEERS INC.
2907 12TH AVE. S.
NASHVILLE TN 37204
PHONE: 615/383-4581
CONTACT: MR. RICK DAVIS

28 AYERST LABORATORIES, INC.
64 MAPLE ST.
ROUSES POINT NY 12979
PHONE: 518/297-6611
CONTACT:

29 B.F. GOODRICH CHEMICAL CO.
6100 OAK TREE BLVD.
CLEVELAND OH 44131
PHONE: 216/279-2697
CONTACT:

30 BARNES-HIND PHARMACEUTICAL
895 KIFER RD.
SUNNYVALE CA 94086
PHONE: 408/736-5462
CONTACT: JANET MCCOMB

31 BARROW-AGEE LABORATORIES INC.
405 SATURN DR. P O BOX 156
MEMPHIS TN 38101
PHONE: 901/332-159
CONTACT: L. HAWKINS

32 BATTELLE COLUMBUS LABORATORY/BIOLOGICAL SCIENCES DEPT.
505 KING AVE.
COLUMBUS OH 43201
PHONE: 614/424-7887
CONTACT: DR. JAY FISHER

33 BATTELLE PACIFIC NORTHWEST DIV.
P O BOX 999
RICHLAND WA 99353
PHONE: 509/942-3602
CONTACT: DR. TARAGANIES

34 BAXTER TRAVENOL INC. TRAVENOL LABORATORIES
6301 LINCOLN AVE.
MORTON GROVE IL 60053
PHONE: 312/965-4700
CONTACT: DR. WHITE

35 BAYVET CORP.
P O BOX 390
SHAWNEE MISSION KS 66201
PHONE: 913/631-4800
CONTACT: DR. SCHMIDL

36 BETZ-CONVERSE-MURDOCH INC.
ONE PLYMOUTH MEETING MALL
PLYMOUTH MEETING PA 19462
PHONE: 215/825-3800
CONTACT: SHARON NORDSTROM

37 BIO-LIFE ASSOCIATES LTD.
P O BOX 124
NEILLSVILLE WI 54456
PHONE: 715/743-4557
CONTACT: DALE FLETCHER

38 BIO-MED RESEARCH LABORATORIES
1115 E. PIKE ST.
SEATTLE WA 98122
PHONE: 206/324-0380
CONTACT: MR. JOHN MAJNARICH

39 BIO-RESEARCH CONSULTANTS
9 COMMERCIAL AVE.
CAMBRIDGE MA 02141
PHONE: 617/864-8735
CONTACT: DR. FRED HOMBURGER

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

40 BIO-SAFETY RESEARCH LABORATORIES
MILK AND BROAD STREETS
BRANCHVILLE NJ 07826
PHONE: 201/948-5454
CONTACT: MR. ROSENFELD

41 BIO-TECHNICS LABORATORIES INC.
1133 CRENSHAW BLVD.
LOS ANGELES CA 90019
PHONE: 213/933-5991
CONTACT: MICHAEL SPECTOR

42 BIO/DYNAMICS INC. TOXICOLOGICAL RESOURCES
METTLERS RD.
EAST MILLSTONE NJ 08873
PHONE: 201/873-2550
CONTACT: GARY BENKE

43 BIOASSAY SYSTEMS CORP.
225 WILDWOOD.
WOBURN MA 01801
PHONE: 617/661-6888
CONTACT: DAVE JOHNSON

44 BIOSCIENCE RESEARCH

CITY OF INDUSTRY CA
PHONE: 213/961-2110
CONTACT:

45 BIOSEARCH INC.
P O BOX 8598
PHILADELPHIA PA 19101
PHONE: 215/848-4459
CONTACT: DR. KARL GABRIEL

46 BIOSPHERICS INC.
4928 WYACONDA RD.
ROCKVILLE MD 20852
PHONE: 301/770-7700
CONTACT: DR. LARRY MERRICKS

47 BIOTICS RESEARCH CORP. INC.
P O BOX 36888
HOUSTON TX 77036
PHONE: 713/789-9020
CONTACT:

48 BORRISTON RESEARCH LABORATORY
5050 BEECH PLACE
TEMPLE HILLS MD 20031
PHONE: 301/899-3536
CONTACT: DR. HELMUTH

49 BRISTOL LABORATORIES
THOMPSON RD. P O BOX 657
SYRACUSE NY 13201
PHONE: 315/432-2000
CONTACT: DR. MADISSOO

50 BRISTOL-MEYERS RESEARCH & DEVELOPMENT LABORATORY
1350 LIBERTY AVE.
HILLSIDE NJ 07207
PHONE: 201/926-6756
CONTACT: DR. V. COTTY

51 BUFFALO TESTING LABORATORIES INC.
902 KENMORE AVE.
BUFFALO NY 14216
PHONE: 716/873-2302
CONTACT: MR. KRIS

52 BURROUGHS WELLCOME CO. TOXICOLOGY & EXPERIMENTAL LAB
CORNWALLIS RD.
RESEARCH TRIANGLE PARK NC 27709
PHONE: 919/541-9090
CONTACT: A. W. MACKLIN

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

53 BUSHY RUN RESEARCH CENTER
R. D. 4 MELLON RD.
EXPORT PA 15632
PHONE: 412/327-1020
CONTACT: DR. FRANK

54 CANNON LABORATORIES
P O BOX 3627
READING PA 19605
PHONE: 215/375-4536
CONTACT: MR. PARKE

55 CAPSULE LABORATORIES
840 SIBLEY MEMORIAL HWY.
ST. PAUL MN 55118
PHONE: 612/457-4926
CONTACT: CLARENCE JOHNSON

56 CARTER WALLACE INC. WALLACE LABORATORIES
HALF ACRE RD.
CRANBURY NJ 08512
PHONE: 609/655-6000
CONTACT: DR. JAMES MCGEE

57 CDC RESEARCH INC.
RT. 632 P O BOX 359
CLARKS SUMMIT PA 18411
PHONE: 717/586-1106
CONTACT: DR. LARSON

58 CHEMICAL INDUSTRY INSTITUTE OF TOXICOLOGY
P O BOX 12137
RESEARCH TRIANGLE PARK NC 27709
PHONE: 919/541-2070
CONTACT: DR. HAMM

59 CHEMICAL SERVICE LABORATORY INC.
P O BOX 220 3408 INDUSTRIAL PKWY.
JEFFERSONVILLE IN 47130
PHONE: 812/282-1359
CONTACT: MR. E.V. ELDER

60 CHEMIE RESEARCH AND MANUFACTURING CO. INC.
160 CONCORD DR.
CASSELBERRY FL 32707
PHONE: 305/831-4519
CONTACT:

61 CHEVRON RESEARCH CO.
576 STANDARD AVE. RM. 5201
RICHMOND CA 94802
PHONE: 415/237-4411
CONTACT:

62 CIBA-GEIGY CORP.
556 MORRIS AVE.
SUMMIT NJ 07901
PHONE: 201/277-5000
CONTACT: DR. DIENER

63 CIBA-GEIGY CORP. AGRICULTURE DIV.
410 SWING RD.
GREENSBORO NC 27409
PHONE: 919/292-7100
CONTACT: DR. STEVENS

64 CLINICAL RESEARCH ASSOC.
50 MADISON AVE.
NY NY 10010
PHONE: 212/685-8789
CONTACT:

65 COLGATE-PALMOLIVE CO.
909 RIVER RD.
PISCATAWAY NJ 08854
PHONE: 201/463-1212
CONTACT: DR. GENE HUDSON

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

66 COMMONWEALTH LABORATORY INC.
2209 E. BROAD ST.
RICHMOND VA 23223
PHONE: 804/648-8358
CONTACT: MR. R. HAWKINS

67 CONTRACTORS AND ENGINEERS SERVICES INC.
606 N. JOHN ST. P O BOX 762
GOLDSBORO NC 27530
PHONE: 919/735-7355
CONTACT: SHERRY GRACY

68 CONTROLS FOR ENVIRONMENTAL POLLUTION INC.
1925 ROSINA
SANTA FE NM 87502
PHONE: 505/982-9841
CONTACT: JIM MUELLER

69 D. W. RYCKMAN AND ASSOCIATES
P O BOX 27310
ST. LOUIS MO 63141
PHONE: 314/569-0991
CONTACT: MR. JEFF PETERS

70 DALLAS LABORATORIES
1323 WALL
DALLAS TX 75215
PHONE: 214/421-1400
CONTACT: BOB BENNETT

71 DAWSON RESEARCH CORP.
P O BOX 30666
ORLANDO FL 32862
PHONE: 305/851-3110
CONTACT: CHARLES BURNS

72 DETROIT TESTING LABORATORY
8720 NORTHEND
OAK PARK MI 48237
PHONE: 313/398-2100
CONTACT: JOHN WOLLBERG

73 DIAGNOSTIC DATA INC.
518 LOGUE AVE.
MOUNTAIN VIEW CA 94043
PHONE: 415/964-7676
CONTACT: DR. M. SAIFER

74 DIAMOND SHAMROCK CORP. T.R. EVANS RESEARCH CENTER
P O BOX 348 OHIO RT. 44 & AUBURN RD.
PAINESVILLE OH 44077
PHONE: 216/357-3700
CONTACT: DR. JOE IGNATOWSKI

75 DIVERSIFIED LABORATORIES INC.
FAIRFAX CIRCLE BLDG. 3251 OLD LEE HWY.
FAIRFAX VA 22030
PHONE: 703/273-2011
CONTACT: MR. JERRY SLONER

76 DOW CHEMICAL CO. PATHOLOGY-TOXICOLOGY DEPT.
P O BOX 68511
INDIANAPOLIS IN 46268
PHONE: 317/873-7000
CONTACT: DR. S. D. WARNER

77 DOW CHEMICAL CO. RESEARCH & DEVELOPMENT USA
1803 BLDG. (47)
MIDLAND MI 48640
PHONE: 517/636-1000
CONTACT: DR. WATANABE

78 DOW CHEMICAL CO. TEXAS DIV. RESEARCH & DEVELOPMENT
FREEPORT TX 77541
PHONE: 713/238-2011
CONTACT:

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79 DOW CORNING CORP.
SOUTH SAGINAW RD.
MIDLAND MI 48640
PHONE: 517/496-5047
CONTACT: MR. CHUCK GROH

80 DRACKETT RESEARCH & DEVELOPMENT LABORATORY
5020 SPRING GROVE AVE.
CINCINNATI OH 45232
PHONE: 513/632-1500
CONTACT: MR. DAVE PERKINS

81 DUPONT HASKELL LABORATORY FOR TOXICOLOGY & INDUS. MEDICINE
ELKTON RD.
NEWARK DE 19711
PHONE: 302/366-5264
CONTACT: B. MCKUSICK

82 EASTMAN KODAK CO. HEALTH,SAFETY & HUMAN FACTORS LABORATORY
KODAK PARK
ROCHESTER NY 14650
PHONE: 716/722-2756
CONTACT: C. J. TERHAAR

83 ECKRICH, PETER, & SONS INC.
1025 OSAGE ST.
FORT WAYNE IN 46802
PHONE: 219/481-2034
CONTACT: DR. DRAUCT

84 EDNAWOOD LABORATORIES
4820 OLD SPANISH TRAIL
HOUSTON TX 77021
PHONE: 713/747-7271
CONTACT: MRS. ALICE PERRY

85 EG & G MASON RESEARCH INSTITUTE
57 UNION ST.
WORCESTER MA 01608
PHONE: 617/791-0931
CONTACT: V. ROBERTS

86 EG&G BIONOMICS AQUATIC TOXICOLOGY LABORATORY
790 MAIN ST.
WAREHAM MA 02571
PHONE: 617/295-2550
CONTACT: BOB FOSTER

87 EG&G BIONOMICS MARINE RESEARCH LABORATORY
BOX 1002 RT. 6
PENSACOLA FL 32507
PHONE: 904/492-0515
CONTACT: MR. ROD PARRIS

88 EG&G MASON RESEARCH INSTITUTE
1530 E. JEFFERSON ST.
ROCKVILLE MD 20852
PHONE: 301/770-4400
CONTACT: DR. STEVE HAWORTH

89 ELARS BIORESEARCH LABORATORY
225 COMMERCE DR.
FORT COLLINS CO 80521
PHONE: 303/221-2050
CONTACT: DR. BECK

90 ELI LILLY & CO.
P O BOX 618 740 S. ALABAMA
INDIANAPOLIS IN 46206
PHONE: 317/261-2000
CONTACT: HAROLD WATH

91 ELI LILLY & CO. ELANCO PRODUCTS DIV.

GREENFIELD IN 46140
PHONE: 317/462-8306
CONTACT: DR. AMUNDSEN

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

92 ENDO LABORATORIES
1000 STEWART AVE.
GARDEN CITY NY 11533
PHONE: 516/832-2148
CONTACT: DR. ROBERT CLARK

93 ENERGY RESOURCES CO. INC.
185 ALEWIFE BROOK PKWY
CAMBRIDGE MA 02138
PHONE: 617/661-3111
CONTACT: DR. PETER SOUW

94 ENVIRO PACT INC.
815 W. 18TH
HIALEAH FL 33010
PHONE: 305/885-1869
CONTACT: MR. MURPHY

95 ENVIRO-MED LABORATORIES INC.
414 W. CALIFORNIA
RUSTON LA 71270
PHONE: 318/255-0060
CONTACT:

96 ENVIRO-MED LABORATORIES INC.
1874 DALLAS DR.
BATON ROUGE LA 70806
PHONE: 504/928-0232
CONTACT: DR. R. FLOURNOY

97 ENVIRONMENTAL CONSULTANTS INC.
1581 HOSIER RD.
SUFFOLK VA 23434
PHONE: 804/539-2321
CONTACT: KATHY GINGHER

98 ENVIRONMENTAL PROTECTION SYSTEMS INC.
P O BOX 20382 106 UPTON DR.
JACKSON MO 39209
PHONE: 601/922-8242
CONTACT: DR. CORBIN MCGRIFF

99 ESA LABORATORIES
43 WIGGINS AVE.
BEDFORD MS 01730
PHONE: 617/275-0100
CONTACT: DR. GRIFFIN

100 EXXON CORP. RESEARCH AND ENVIRONMENTAL HEALTH DIV.
P O BOX 235
E. MILLSTONE NJ 08873
PHONE: 201/873-6000
CONTACT: GERARD F. EGAN

101 FMC CORP./CHEMICAL DEPT./CORPORATE TOXICOLOGY DEPT.
P O BOX 8
PRINCETON NJ 08540
PHONE: 609/452-2300
CONTACT: DR. FLETCHER

102 FOOD AND DRUG RESEARCH LABORATORIES
P O BOX 107 RT. 17C
WAVERLY NY 14892
PHONE: 607/565-2931
CONTACT:

103 FOOD AND DRUG RESEARCH LABORATORIES INC.
60 EVERGREEN PLACE
EAST ORANGE NJ 07018
PHONE: 201/677-9500
CONTACT: MR. HOWARD FEINMAN

104 FOREMOST-MCKEESON INC. MCKEESON LABORATORIES
424 GRASMERE AVE.
FAIRFIELD CT 06430
PHONE: 203/259-1661
CONTACT:

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

105 FRANKLIN LABORATORIES DIV./DENVER LABORATORY
4238 YORK
DENVER CO 80216
PHONE: 303/629-6636
CONTACT: DAVE SHEETS

106 FREDERICK CANCER RESEARCH CENTER
P O BOX B
FT. DETRICK MD 21701
PHONE: 301/663-8000
CONTACT: DR. SERRANO

107 GENERAL MOTORS RESEARCH LABORATORIES

WARREN MI 48090
PHONE: 313/575-3058
CONTACT: J. VOSTAL

108 GENEX CORP.
6110 EXECUTIVE BLVD. SUITE 1090
ROCKVILLE MD 20852
PHONE: 301/770-0650
CONTACT: MRS. A. MEYERS

109 GHT LABORATORIES OF IMPERIAL VALLEY INC.
106 S. EIGHTH ST.
BRAWLEY CA 92227
PHONE: 714/344-2532
CONTACT: LINDA CONNAWAY

110 GIBRALTAR BIOLOGICAL LABORATORIES
23 JUST RD.
FAIRFIELD NJ 07066
PHONE: 201/227-6882
CONTACT: DR. HERBERT PRINCE

111 GILBERT ASSOCIATES INC. LABORATORY SERVICES
30 NOBLE ST. P O BOX 1498
READING PA 19602
PHONE: 215/775-2600
CONTACT: MR. BOB LARGE

112 GILLETTE CO.
1413 RESEARCH BLVD.
ROCKVILLE MD 20850
PHONE: 617/268-3200
CONTACT: LOU DIPASQUALE

113 GOLD KIST RESEARCH CENTER
2230 INDUSTRIAL BLVD.
LISHONIA GA 30058
PHONE: 404/482-7466
CONTACT: DR. JOHN ESKEN

114 GOODYEAR TIRE & RUBBER CO.
1144 E. MARKET ST.
AKRON OH 44316
PHONE: 216/796-7445
CONTACT: MR. C. BOHLMAN

115 GULF SCIENCE AND TECHNOLOGY CO. LIFE SCIENCES LABORATORIES
P O BOX 3240
PITTSBURGH PA 15230
PHONE: 412/665-6000
CONTACT: DR. HAROLD MCFARLAND

116 GULF SOUTH RESEARCH INSTITUTE
P O BOX 1177
NEW IBERIA LA 70126
PHONE: 318/365-2411
CONTACT: DR. BILL GREER

117 HAHNEMANN MEDICAL COLLEGE & HOSPITAL
230 N. BROAD ST.
PHILADELPHIA PA 19102
PHONE: 215/448-8237
CONTACT: DR. CALESNICK

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

118 HALLOWELL LABORATORIES PRODUCT INVESTIGATIONS INC.
151 E. TENTH AVE.
CONSHOHOCKEN PA 19428
PHONE: 215/825-8210
CONTACT: DR. SHELANSKI

119 HAZLETON LABORATORIES
9200 LEESBURG TURNPIKE
VIENNA VA 22180
PHONE: 703/893-5400
CONTACT: MR. LEE VARDEN

120 HILL-TOP RESEARCH
HWY. 126
MIAMIVILLE OH 45147
PHONE: 513/831-3114
CONTACT: DAVID CONINE

121 HOLLISTER-STIER LABORATORIES
BOX 3145 TERMINAL ANNEX
SPOKANE WA 89220
PHONE: 509/489-5656
CONTACT: DON CLARIDGE

122 HOWARD UNIVERSITY MEDICAL SCHOOL/DEPT. OF PHARMACOLOGY

WASHINGTON DC 20059
PHONE: 202/636-6311
CONTACT: DR. WILLIAM WEST

123 ICI AMERICAS BIOMEDICAL RESEARCH DEPT.
NEW MURPHY RD. & CONCORD PK.
WILMINGTON DE 19897
PHONE: 302/575-8021
CONTACT: DR. KLAUS HUBBEN

124 IMS AMERICA LTD. ENVIRONMENTAL RESOURCES GROUP
MAPLE AVE. & BUTLER PIKE
AMBLER PA 19002
PHONE: 215/643-0400
CONTACT: AURORA CHANG

125 INDEPENDENT EQUIPMENT CORP./RECON SYSTEMS INC.
51 FIFTH ST. P O BOX 842
SOMERVILLE NJ 08876
PHONE: 201/685-0442
CONTACT: MR. TORO

126 INDUSTRIAL LABORATORIES
3001 CULLEN ST.
FORT WORTH TX 76107
PHONE: 817/332-2259
CONTACT: MR. RANDY CAHOON

127 INDUSTRIAL LABORATORIES CO., THE
1450 E. 62ND AVE.
DENVER CO 80216
PHONE: 303/287-9691
CONTACT: MR. PAUL OCHS

128 INHALATION TOXICOLOGY RESEARCH INSTITUTE
P O BOX 5890
ALBUQUERQUE NM 87115
PHONE: 505/264-6835
CONTACT: DR. R. MCCLELLAN

129 INSTITUTE FOR MEDICAL RESEARCH
COPEWOOD AND DAVIS STREETS
CAMDEN NJ 08103
PHONE: 609/966-7377
CONTACT: DR. L. CORIELL

130 INSTITUTE FOR RESEARCH INC.
8330 WESTGLEN DR.
HOUSTON TX 77063
PHONE: 713/783-8400
CONTACT: MR. PHILLIP THOMAS

TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

131 INTERNATIONAL MINERALS & CHEMICAL CORP. IMC TECHNICAL CENTER
1331 S. FIRST ST.
TERRE HAUTE IN 47808
PHONE: 812/232-0121
CONTACT: MS. JESSIE WILBUR

132 INTERNATIONAL RESEARCH & DEVELOPMENT CORP.
500 N. MAIN ST.
MATTAWAN MI 49071
PHONE: 616/668-3336
CONTACT: DR. GOLDENTHAL

133 INTERX RESEARCH CORP.
2201 W. 21ST ST.
LAWRENCE KS 66044
PHONE: 916/841-1700
CONTACT:

134 INVERESK RESEARCH INTERNATIONAL/K. J. O'CONNOR ASSOC.
K. STREET NW SUITE 334
WASHINGTON DC 20005
PHONE: 202/638-2652
CONTACT: MR. K.J. O'CONNOR

135 JEFFERSON PROFESSIONAL SERVICES
P O BOX 3397
LITTLE ROCK AR
PHONE: 501/374-1296
CONTACT: SHIRLEY LOUIE

136 JOHNSON & JOHNSON BABY PRODUCTS LABORATORY
GRANDVIEW RD.
SKILLMAN NJ 08558
PHONE: 201/874-1461
CONTACT: MR. MIKE CHECKAWSKI

137 JONES, EDMONDS & ASSOCIATES
730 N. WALDO RD.
GAINESVILLE FL 32601
PHONE: 904/377-5821
CONTACT:

138 JRB ASSOCIATES INC.
8400 WESTPARK DR.
MCLEAN VA 22101
PHONE: 703/821-4600
CONTACT: MR. MIKE HIGGINS

139 KANSAS STATE UNIV./COMPARATIVE TOXICOLOGY LABORATORIES
SCHOOL OF VETERINARY MEDICINE
MANHATTAN KS 66506
PHONE: 913/532-5679
CONTACT: DR. FRED OEHME

140 KEM-TECH LABORATORIES
16550 HIGHLAND RD.
BATON ROUGE LA 70209
PHONE: 504/293-8650
CONTACT: MR. ARTIMELEE

141 KENDALL CO. RESEARCH CENTER
411 LAKE ZURICH RD.
BARRINGTON IL 60010
PHONE: 312/381-0370
CONTACT: DR. MILLER

142 LABORATORY RESEARCH ENTERPRISES
6321 S. SIXTH ST.
KALAMAZOO MI 49001
PHONE: 616/375-0482
CONTACT: DR. J. MEHRING

143 LANCASTER LABORATORIES INC.
5424 BUCHANAN TRAIL EAST P O BOX 467
WAYNESBORO PA 17268
PHONE: 717/762-9127
CONTACT: MR. HOWARD HOLZMAN

144 LAUCKS TESTING LABORATORIES INC.
1008 WESTERN AVE.
SEATTLE WA 98104
PHONE: 202/622-0727
CONTACT: J. M. OWENS

145 LAW & CO. OF WILMINGTON
P O BOX 629
WILMINGTON NC 28401
PHONE: 919/762-7082
CONTACT:

146 LEBERCO LABORATORIES
123 HAWTHORNE ST.
ST. ROSELLE PARK NJ 07204
PHONE: 201/245-1933
CONTACT: DR. I. LEVENSTEIN

147 LEE PHARMACEUTICALS
1444 SANTA ANITA AVE.
SOUTH EL MONTE CA 91733
PHONE: 213/442-3141
CONTACT: DR. DIANE TIEGLER

148 LEVER BROTHERS TOXICOLOGY SECTION
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EDGEWATER NJ 07020
PHONE: 201/943-7100
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149 LFE CORP. ENVIRONMENTAL ANALYSIS LABORATORIES
2030 WRIGHT AVE.
RICHMOND CA 94804
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CONTACT: DICK GERCIS

150 LITRON LABORATORIES LTD.
1351 MOUNT HOPE AVE.
ROCHESTER NY 14620
PHONE: 716/275-4008
CONTACT: DR. ANDREW TOMEISKO

151 LITTON BIONETICS INC.
5516 NICHOLSON LN.
KENSINGTON MD 20795
PHONE: 301/881-5600
CONTACT: DR. ROBERT WEIR

152 MALCOM PIRNIE INC.
2 CORPORATE PARK DR.
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153 MASSACHUSETTS INSTITUTE OF TECHNOLOGY/NUTRITION & FOOD SCI.
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CONTACT: DR. TILLY

154 MCNEIL PHARMACEUTICALS

SPRINGHOUSE PA 14774
PHONE: 215/628-5000
CONTACT: DR. MILLER

155 MEDICAL COLLEGE OF VIRGINIA/DEPT. OF PHARMACOLOGY
MCV/VCU/HSD BOX 762
RICHMOND VA 23298
PHONE: 804/786-0329
CONTACT: DR. J. BORZELLECA

156 MEDTRONICS INC.
3055-T OLD HWY 8
MINNEAPOLIS MN 55418
PHONE: 612/574-4000
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TOXICOLOGY TESTING LABORATORIES -- ALPHABETICAL LISTING

157 MEI-CHARLTON INC.
2233 SW CANYON RD.
PORTLAND OR 97201
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CONTACT: MR. DON VALLEY

158 MELOY LABORATORIES
6715 ELECTRONIC DR.
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PHONE: 703/354-2600
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159 MERRELL NATIONAL LABORATORIES/CINCINNATI LABORATORY
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CINCINNATI OH 45215
PHONE: 513/948-9111
CONTACT:

160 METRO-SERVICES LABORATORY
235 E. BURNETT AVE.
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PHONE: 502/635-5463
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161 MICROBIOLOGICAL AND BIOCHEMICAL ASSAY LABORATORIES INC.
P O BOX 9461
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CONTACT: MR. HERMAN KESSE

162 MICROBIOLOGICAL ASSOCIATES
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BETHESDA MD 20116
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163 MIDECO
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164 MIDWEST RESEARCH INSTITUTE
425 VOLKER BLVD.
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165 MILES LABORATORIES INC. CONSUMER PRODUCTS DIV.
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ELKHART IN 46514
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166 MOBAY CHEMICAL CORP. RESEARCH CENTER
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167 MOBIL RESEARCH & DEVELOPMENT
150 E. 42ND ST.
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168 MONSANTO ENVIRONMENTAL HEALTH LABORATORY
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169 MONSANTO RESEARCH CORP. DAYTON LABORATORY
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170 MOTE MARINE LABORATORY INC.
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171 MOUNT DESERT ISLAND BIOLOGICAL LABORATORY
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172 MOUTREY & ASSOCIATES INC.
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173 NATIONAL MEDICAL SERVICES INC.
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174 NATIONAL TECHNICAL SYSTEMS TESTING DIV.
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CONTACT: DR. PAUL

175 NEW ENGLAND RESEARCH INC.
15 SAGAMORE RD.
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PHONE: 617/752-0346
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176 NORTH AMERICAN SCIENCE ASSOCIATES
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PHONE: 419/666-9455
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177 NORTHROP SERVICES INC.
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178 NORTHROP SERVICES INC.
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179 NUTRITION INTERNATIONAL INC./PRODUCT SAFETY LABORATORIES
725 CRANBERRY RD.
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PHONE: 201/545-1704
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180 O A LABORATORIES INC.
1437 SADLIER CR. WEST DR.
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PHONE: 317/353-9721
CONTACT: DR. WILLIAM CATESS

181 OMAHA CHEMICAL & ENVIRONMENTAL TESTING
2917 DOUGLAS ST.
OMAHA NE 68131
PHONE: 402/341-5181
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182 OMNI RESEARCH INC.
4800 RALENEL AVE
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183 OREGON STATE UNIV./OAK CREEK LABORATORIES OF BIOLOGY
CORVALLIS OR 97331
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184 ORMONT DRUG & CHEMICAL CO., INC. PANRAY DIV.
16600 NW 54TH AVE.
MIAMI FL 33014
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CONTACT:

185 ORTHO PHARMACEUTICAL CORP.
RT. 202
RARITAN NJ 08869
PHONE: 201/524-0400
CONTACT: DR. MCGUIRE

186 ORTHO RESEARCH INSTITUTE OF MEDICAL SCIENCES
RT. 202
RARITAN NJ 08869
PHONE: 201/524-2735
CONTACT:

187 OXFORD CHEMICAL DIV.
P O BOX 80202
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188 PACE LABORATORY
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189 PARAMETRIX INC.
13020 NORTHRUP WAY SUITE 8
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190 PARKE-DAVIS PHARMACEUTICAL RESEARCH DIV.
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191 PASAT RESEARCH ASSOCIATION INC.
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192 PATTISON'S LABORATORIES INC.
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193 PCR INC.
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194 PFIZER INC. CENTRAL RESEARCH
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197 PHARMAKON LABORATORIES
WAVERLY PA 18471
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198 PHARMI-CHEM TESTING
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199 PHYSIOLOGICAL RESEARCH LABORATORY
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201 PRINCETON TESTING LABORATORY
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202 PROCTOR & GAMBLE
301 E. SIXTH ST.
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203 PURDUE UNIV./DEPT. OF PHARMACOLOGY AND TOXICOLOGY
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204 RALSTON PURINA CENTRAL RESEARCH LABS & RESEARCH SERVICES
CHECKERBOARD SQ.
ST. LOUIS MO 63188
PHONE: 314/982-0111
CONTACT:

205 RALSTON PURINA RESEARCH FARM
RT. 2
GRAY SUMMIT MO 63039
PHONE: 314/982-1000
CONTACT:

206 RALTECH SCIENTIFIC SERVICES
BOX 7545 3301 KINSMAN BLVD.
MADISON WI 53701
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CONTACT: MR. ROBERT FISHBECK

207 RANDOLPH & ASSOC. INC.
8901 N. INDUSTRIAL RD.
PEORIA IL 61615
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CONTACT: MR. KIRK SWEETLAND

208 REDKEN LABORATORIES INC.
14721 CALIFA ST.
VAN NUYS CA 91401
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209 REED, JAMES R., & ASSOCIATES INC.
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210 REVLON RESEARCH CENTER INC.
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211 RIEKE, CARROLL, MULLER & ASSOCIATES
P O BOX 130
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212 ROHM & HAAS CO.
P O BOX 18183
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213 SAFETY SPECIALISTS INC.
3284F EDWARD AVE.
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214 SALK INSTITUTE FOR BIOLOGICAL STUDIES
10010 N. TORREY PINES RD.
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215 SANDERS MEDICAL RESEARCH FOUNDATION INC.
33 SE 3RD ST.
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216 SANDOZ PHARMACEUTICALS, PRECLINICAL SAFETY ASSESSMENT DEPT.
RT. 10
HANOVER NJ 07936
PHONE: 201/386-8309
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217 SCHERING-PLOUGH CORP.
RT. 94
LAFAYETTE NJ 07848
PHONE: 201/931-2000
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218 SCIENTIFIC ASSOCIATES INC.
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219 SCOTT, DWIGHT G., RESEARCH CENTER
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220 SEARLE, G.D., AND CO. SEARLE LABORATORIES
P O BOX 5110
SKOKIE IL 60680
PHONE: 312/982-7000
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221 SEAWAY INDUSTRIAL LABORATORIES INC.
542-544 CONKEY & JACKSON ST.
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PHONE: 219/932-1770
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REDWOOD CITY CA 94063
PHONE: 415/364-9222
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223 SERCO SANITARY ENGINEERING LABORATORIES INC.
1931 W. COUNTY RD. C-2
ROSEVILLE MN 55113
PHONE: 612/636-7173
CONTACT: MR. RICK DOBEL

224 SHARPS ASSOCIATES
767-B CONCORD AVE.
CAMBRIDGE MA 02138
PHONE: 617/354-2800
CONTACT:

225 SHELL LABORATORIES

HOUSTON TX
PHONE: 713/241-6161
CONTACT: DON STEVENSON

226 SKINNER & SHERMAN LABORATORIES INC.
300 SECOND AVE.
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PHONE: 617/890-7200
CONTACT: MR. HAL DALZELL

227 SMITH KLINE AND FRENCH LABORATORIES
1500 SPRING GARDEN ST.
PHILADELPHIA PA 19101
PHONE: 215/854-4000
CONTACT: DR. KALMAN T. SZABO

228 SMITH KLINE ANIMAL HEALTH RESEARCH CENTER
1600 PAOLI
WESTCHESTER PA 19101
PHONE: 215/854-4000
CONTACT:

229 SMITH KLINE CLINICAL LABORATORY
343 WINTER ST.
WALTHAM MA 02154
PHONE: 617/890-6161
CONTACT:

230 SOUTH MOUNTAIN LABORATORIES
380 LACKAWANNA PL.
SOUTH ORANGE NJ 07079
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CONTACT: MR. MARGIERI

231 SOUTHERN RESEARCH INSTITUTE/KETTERING MEYER LABORATORY
2000 NINTH AVE. S.
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232 SOUTHWEST FOUNDATION FOR RESEARCH AND EDUCATION
P O BOX 28147
SAN ANTONIO TX 78284
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233 SOUTHWEST RESEARCH INSTITUTE
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234 SOUTHWESTERN LABORATORIES
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235 SPRINGBORN GROUP/SPRINGBORN LABORATORIES
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236 SPRINGBORN INSTITUTE FOR BIORESEARCH INC.
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237 SQUIBB, E.R. AND SONS
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238 SRI-INTERNATIONAL
333 RAVENSWOOD AVE.
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CONTACT: DAVID JONES

239 STAUFFER CHEMICAL CO.
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240 STERLING WINTHROP RESEARCH INSTITUTE
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241 STIEFEL LABORATORIES/A.C. STIEFEL RESEARCH INSTITUTE INC.
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242 STILLMEADOW INC.
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PHONE: 713/776-8828
CONTACT:

243 SYRACUSE RESEARCH CORP. CHEMICAL HAZARD ASSESSMENT CENTER
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244 TECHNAM INC.
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CONTACT:

245 TERRALAB
3585 VIA TERRA
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246 THERMO ELECTRON CORP.
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247 THORNTON LABORATORIES ANALYTICAL AND CONSULTING CHEMISTS
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248 TOX MONITOR LABORATORY INC.
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249 TOXICITY RESEARCH LABORATORY
510 W. HACKLEY
MUSKEGON
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250 TOXICON
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BATON ROUGE
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251 TOXIGENICS INC.
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PHONE: 217/875-3930
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252 TPS INC.
P O BOX 333
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IN 47620
PHONE: 812/985-5900
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253 TRC ENVIRONMENTAL CONSULTANTS INC.
125 SILAS DEANE HWY.
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254 TRI-TECH LABORATORIES INC.
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TN 37027
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255 TROJAN LABORATORIES
118 N. FIFTH
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256 U.S. TESTING CO., THE
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258 UNILAB RESEARCH
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262 UPJOHN CO., THE/PHARMACEUTICAL RESEARCH & DEVELOPMENT LAB.
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KALAMAZOO MI 49001
PHONE: 616/323-4000
CONTACT:

263 UTAH BIOMEDICAL TEST LABORATORY
520 WAKARA WAY
SALT LAKE CITY UT 84108
PHONE: 801/581-8267
CONTACT: MR. RAND POTTER

264 VET-A-MIX INC.
604 W. THOMAS
SHENANDOAH IA 51601
PHONE: 712/246-3763
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265 VETPATH - ANIMAL REFERENCE LABORATORY, THE
60 COMMERCE WAY
HACKENSACK NJ 07606
PHONE: 800/631-0883
CONTACT: DR. DAVIS

266 WAYNE STATE UNIV./DEPT. OF OCCUPATIONAL & ENVIRON. HEALTH
625 MULLET
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267 WELLS LABORATORIES INC.
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268 WEST PAINE LABORATORY
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269 WEST VIRGINIA UNIV. MEDICAL CR./DEPT. OF PHARMACOLOGY
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270 WHITMOYER LABORATORIES INC.
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271 WIL RESEARCH LABORATORIES INC.
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272 WILDLIFE INTERNATIONAL LTD.
SOLITUDE CREEK FARM
ST. MICHAELS MD 21663
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273 WINGERTER LABORATORIES INC.
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NORTH MIAMI FL 33161
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CONTACT: MR. MCCABE

APPENDIX B

TOXICOLOGY LABORATORY CONTACT FORM
AND
TELEPHONE SURVEY INSTRUMENT

LABORATORY CONTACT FORM

Initial Contact

Hello, my name is ______________ from the University of Kansas Center for Public Affairs. We are doing a survey for the U.S. Environmental Protection Agency to gather information about the availability of chemical testing services, and the types of tests provided by laboratories.

Does your toxicology laboratory test chemicals for environmental or health effects?

Yes No

IF YES, PROCEED WITH INTERVIEW

IF NO, THANK RESPONDENT AND PUT IN "NOT APPLICABLE" FOLDER

Who would be the best person to provide information regarding these issues?

Name: ________________________________

Is ("Name") in? Yes No

IF YES, PROCEED WITH INTERVIEW

IF NO, ASK WHEN S/HE'LL BE BACK AND MAKE APPOINTMENT ON CALLBACK RECORD

Contact with Actual Respondent

REPEAT FIRST PARAGRAPH "HELLO, MY NAME IS . . ." CONTINUE WITH:

Information collected will be used to develop a list of toxicology laboratories for EPA. This will improve the understanding of chemical testing laboratories which will be helpful in assessing testing availability. Your laboratory was chosen because it appeared on _______, a publicly available list. Your responses are completely confidential and your cooperation is of course, voluntary. First of all, . . .

PROCEED WITH INTERVIEW, QUESTION 1

IF RESPONDENT DOES NOT HAVE TIME FOR A 15 - 20 MINUTE INTERVIEW, MAKE ARRANGEMENTS TO CALL BACK ON THE COVER SHEET. DON'T ASK IF THEY HAVE TIME, THEY WILL TELL YOU IF THEY DON'T

Part II. OMB Approval No. 2000-0141

EPA Toxicology Laboratory Survey

A. GENERAL

1. In which of the following areas does your laboratory currently perform chemical testing: (circle response)

Area *	Q.1 Perform Yes	Q.1 Perform No	Q.2 Percent of Volume
Mammalian Testing	1	2	_____
In-Vitro Testing	1	2	_____
Environmental Effects Testing	1	2	_____
Chemical Fate Testing	1	2	_____
Product and Analytical Testing	1	2	_____
(* See questions B.1, C.1, etc.)	(Q.A.2) Total Vol.		100%

2. What percent of your total laboratory testing volume (Dollars) is in each of the areas designated above (Q.A.1)?

3. What percent of your total laboratory testing ---

	Percent%
(a) is on contract?	_____
(b) is in-house (captive)?	_____
	100%

4. Approximately how many total persons, on the average, did your laboratory employ in 1980?

(Include professionals--toxicologists, pathologists--, technicians, management and administrative, and other staff)

Total Persons _____

5. Approximately how many of these employees were---

Professionals?	_____
Technicians?	_____
Management & Administrative?	_____
Other Staff?	_____
Check Total (See A.4.)	☐

6. Also, as a genaral measure, how many square-feet of toxicology laboratory space do you have at this facility?

Square Feet _____

7. (If the answer to Mammalian Testing in Question A.1 is no, then ask:) Do you plan to add Mammalian Testing capability within the next 1-2 years?

Addition Yes	Addition No
1	2

If "yes", go to Question B.4 and B.5

B. MAMMALIAN TESTING (If Performed--See Q.A.1)

1. Which of the following specific types of Mammalian Testing can be performed currently (with available resources) in your laboratory -- (circle response)

		Current Capability	
		Yes	No
(a) Acute Testing			
Acute oral toxicity		1	2
Acute dermal toxicity		1	2
Acute inhalation toxicity		1	2
Primary eye irritation		1	2
Primary dermal irritation		1	2
Dermal sensitization		1	2
Acute delayed neurotoxicity		1	2
(b) Subchronic Testing			
Subchronic oral dosing		1	2
Subchronic 90-day dermal toxicity		1	2
Subchronic inhalation toxicity		1	2
Subchronic neurotoxicity		1	2
(c) Chronic Testing			
Chronic--oral	(Route/Technique)	1	2
Chronic--dermal		1	2
Chronic--inhalation		1	2
Chronic--parenteral		1	2
(d) Reproduction (e.g., 3 generation)		1	2
(e) Teratogenic		1	2
(f) Oncogenic		1	2
(g) Histopathology		1	2
(h) Other (Name)			
____________________		1	2
____________________		1	2

2. Does your laboratory have the capacity to do additional mammalian testing? (Annual rate, as compared to 1980)

Additional Capacity	
Yes	No
1	2

(If yes): About what percent more testing could be performed?

	Percent Range
1-10%	1
11-20%	2
21-30%	3
More than 30%	4

3. (a) Which of the following test animals are you capable of using currently in your laboratory?

Test Animal (species)	Animals Used Yes	Animals Used No	Ave. No. at Lab	Max. No. Possible
Rodents (mice, rats, hamsters, gerbils	1	2	______	______
Rabbits	1	2	______	______
Guinea Pigs	1	2	______	______
Dogs	1	2	______	______
Cats	1	2	______	______
Primates	1	2	______	______
Poultry	1	2	______	______
Large Domestic Animals	1	2	______	______

(b) For each test animal used, how many would you normally have at your laboratory both in tests and in inventory? (Ave. No. above)

(c) Also, for each test animal used, what is the maximum number that you could keep in tests or in inventory? (Max. No. above)

(d) Are any of the test animals named above, or others, in short supply?

	Short Supply Yes	Short Supply No	Short Supply Don't Know
	1	2	3

(If yes) which ones?

____

____

4. A number of general factors have been cited in publications as factors that could constrain the expansion of toxicology testing in the U.S. From the perspective of your laboratory how critical are each of the following factors on a scale of 1 to 7 where 1 is not critical and 7 is very critical.

Factor	Rating: Not Critical <———> Very Critical						
	1	2	3	4	5	6	7
(a) No. of Available Professionals	1	2	3	4	5	6	7
If (a) is rated 4 to 7, also rate the following:							
• Toxicologists	1	2	3	4	5	6	7
• Veterinary Pathologists	1	2	3	4	5	6	7
• Pathologists	1	2	3	4	5	6	7
(b) Availability of Animals	1	2	3	4	5	6	7
(c) Availability of Equipment	1	2	3	4	5	6	7
(d) Availability of Supplies	1	2	3	4	5	6	7
(e) Availability of Laboratory Space	1	2	3	4	5	6	7
(f) Availability of Capital	1	2	3	4	5	6	7
(g) Other (specify)							
______________	1	2	3	4	5	6	7
______________	1	2	3	4	5	6	7

5. Which of these factors is the most critical constraint to the expansion of your toxicological testing capacity?

Most Critical Factor

____

This concludes our questions on Mammalian Testing.

C. IN-VITRO TESTING (If Performed--See Q.A.1)

1. Which of the following In-Vitro tests can be performed currently (with available resources) in your laboratory---

	Tests	Current Capability	
		Yes	No
(a)	Tests for Detecting Gene Mutations (e.g., Ames Test, Mouse Lymphoma Assay)	1	2
(b)	Tests for Detecting Chromosomal Aberrations (e.g., Cytogenetics, Dominant Lethal Assay)	1	2
(c)	Tests for Detecting Primary DNA Damage (e.g., DNA Repair, Unscheduled DNA Synthesis)	1	2
(d)	Tests of Physiological Parameters (e.g., Biochemical, Cytology)	1	2

2. Does your laboratory have the capacity to do additional In-Vitro testing?

Additional Capacity	
Yes	No
1	2

(If yes): About what percent more testing could be performed,

	Percent Range
1-10%	1
11-20%	2
21-30%	3
More than 30%	4

D. ENVIRONMENTAL EFFECTS TESTING (If Performed--See Q.A.1)

1. Is your laboratory currently capable of performing---

		Current Capacity	
		Yes	No
(a)	terrestrial testing?	1	2
(b)	aquatic testing?	1	2

2. Does your laboratory have the capacity to do additional environmental effects testing?

Additional Capacity	
Yes	No
1	2

(If yes): About what percent more testing can be performed,

	Percent Range
1-10%	1
11-20%	2
21-30%	3
More than 30%	4

E. CHEMICAL FATE TESTING (If Performed--See Q.A.1)

1. Which of the following types of chemical fate studies can be performed currently---

	Current Capability Yes	 No
(a) laboratory studies (e.g. hydrolysis, photodegradation, soil metabolism)	1	2
(b) field studies (e.g. field dissipation, bioaccumulation)	1	2

2. Does your laboratory have the capacity to do additional chemical fate testing?

Additional Capacity Yes	 No
1	2

(If yes): About what percent more testing could be performed,

	Percent Range
1-10%	1
11-20%	2
21-30%	3
More than 30%	4

F. SOURCES OF DEMAND FOR TESTING (OPTIONAL--OMIT IF TIME IS LIMITED)

1. Approximately what percent of your laboratory's testing is performed in response to the following:

	Percent
EPA - Toxic Substances Control Act (TSCA)	______
EPA - Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)	______
EPA - Resource Conservation and Recovery Act (RCRA)	______
Food and Drug Administration (FDA)	______
National Institute for Environmental Health Science (NIEHS)	______
National Cancer Institute (NCI)	______
Consumer Products Safety Commission (CPSC)	______
Occupational Safety and Health Act (OSHA)	______
OTHER:	______
______________________________	______
______________________________	______
______________________________	______

That concludes the specific questions. Would you please send us a brochure, annual report, or any other information which you have readily available, which describes the types of services performed by your laboratory? In addition, could you identify any new testing laboratories of which you are aware?

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Thank you for your cooperation.